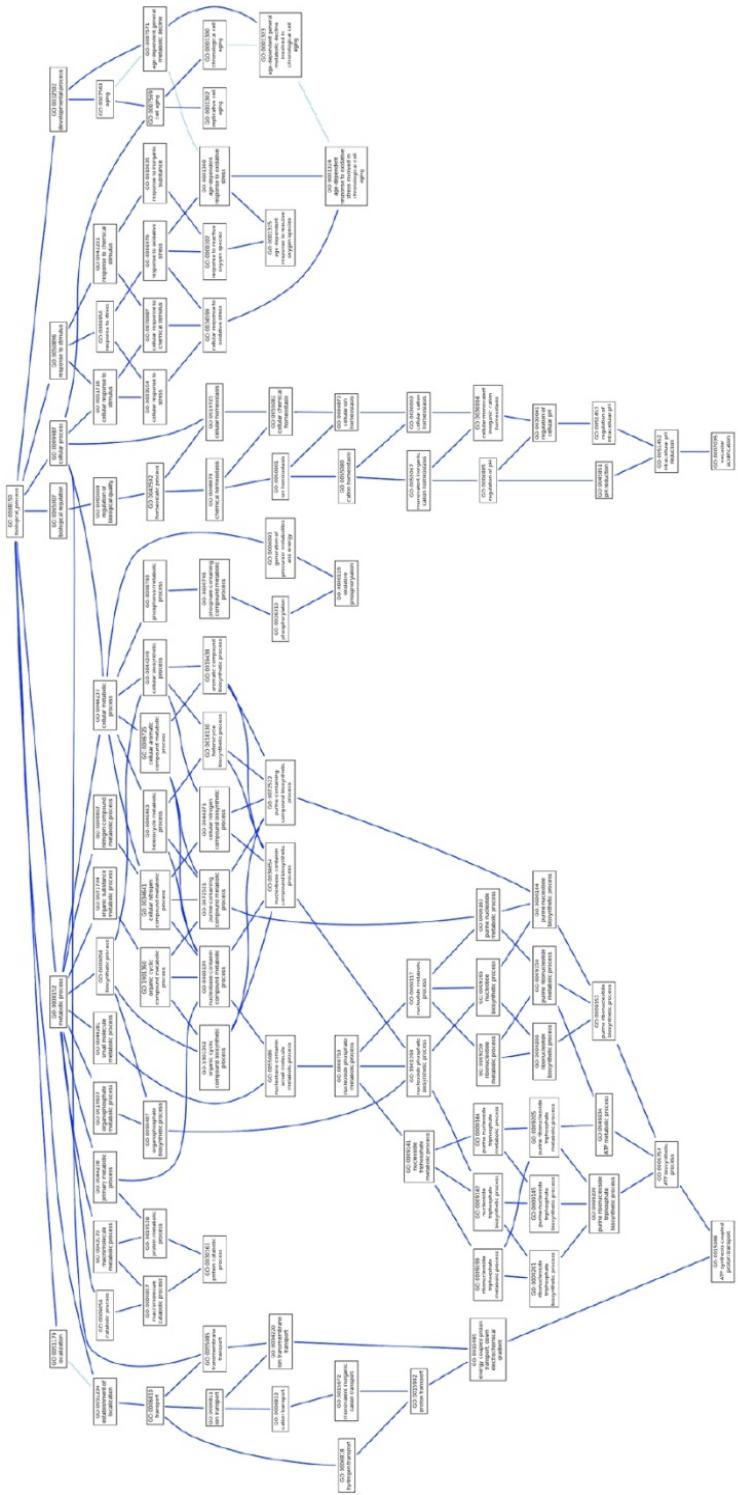
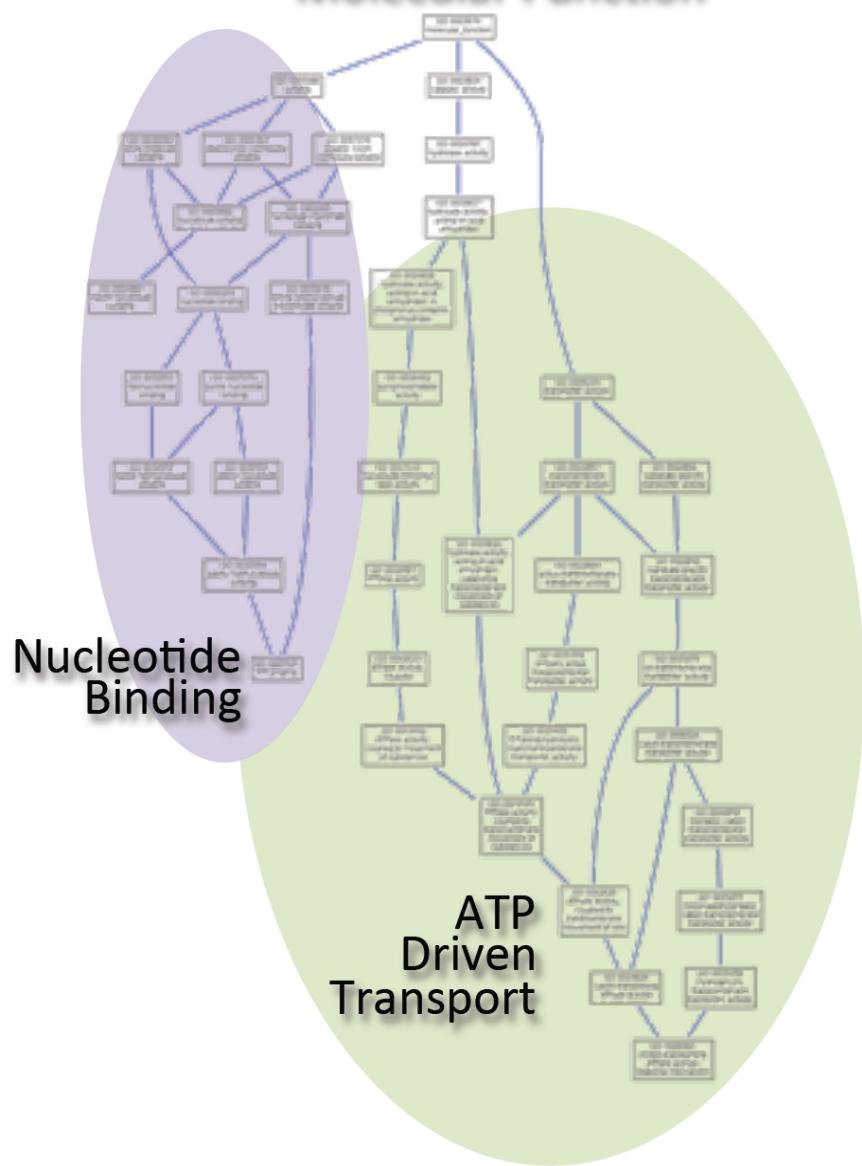


Supplemental Figure 1 – Absolute changes in RLS among Single Gene Mutants on DR. (A) Absolute change in RLS in 166 single deletion strains subjected to a reduction in media glucose (Glu) to 0.05%. The observed variation was independent of both mean RLS (B) and growth rate (C) on 2% glucose. Summary data and statistics are presented in Table S1.

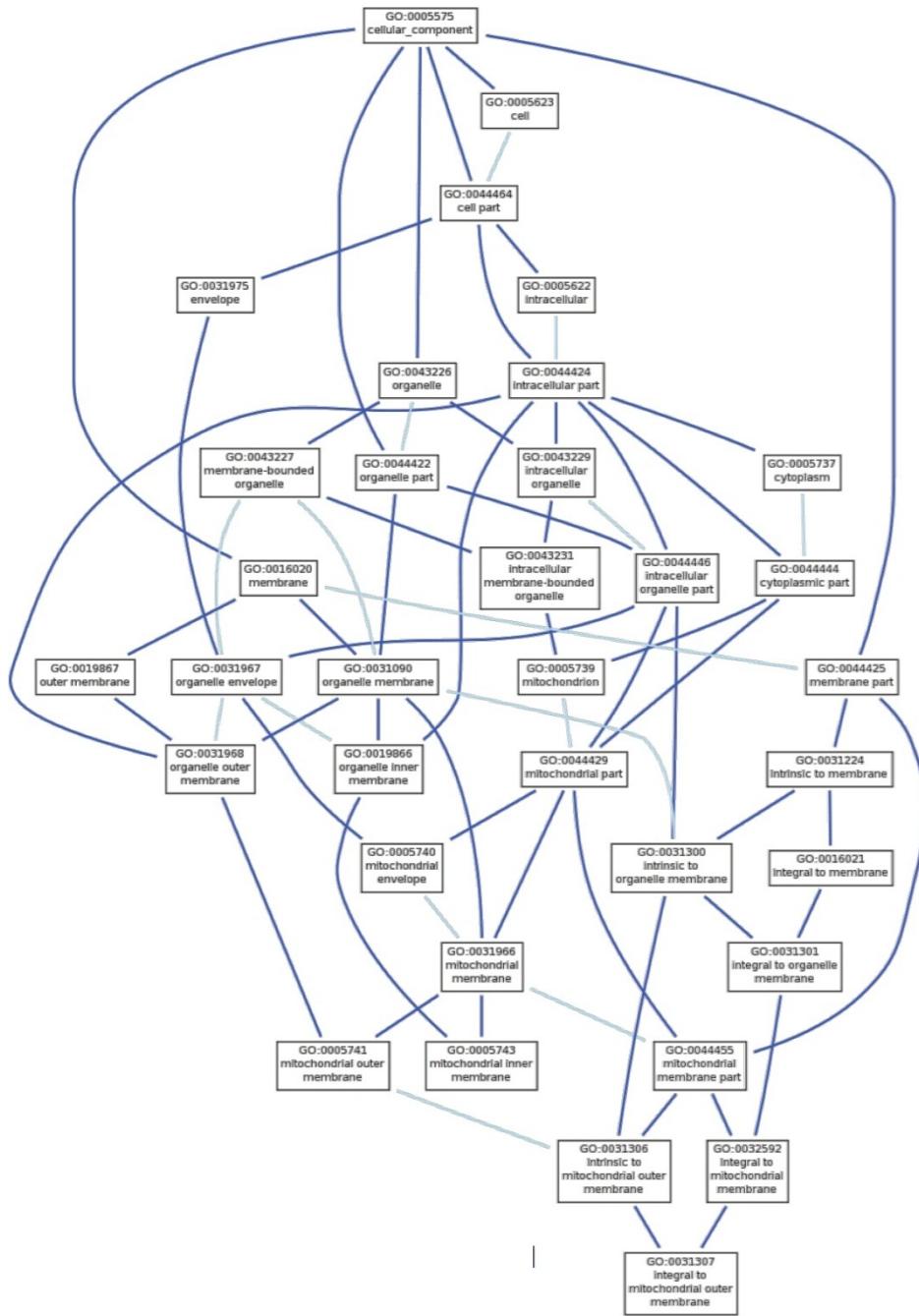
Supplemental Figure 2 – AMIGO Visualization of GO Pathways Significantly Enriched in Mutants with RLS Significantly Decreased by DR. Summary data is presented in Tables S3-5.



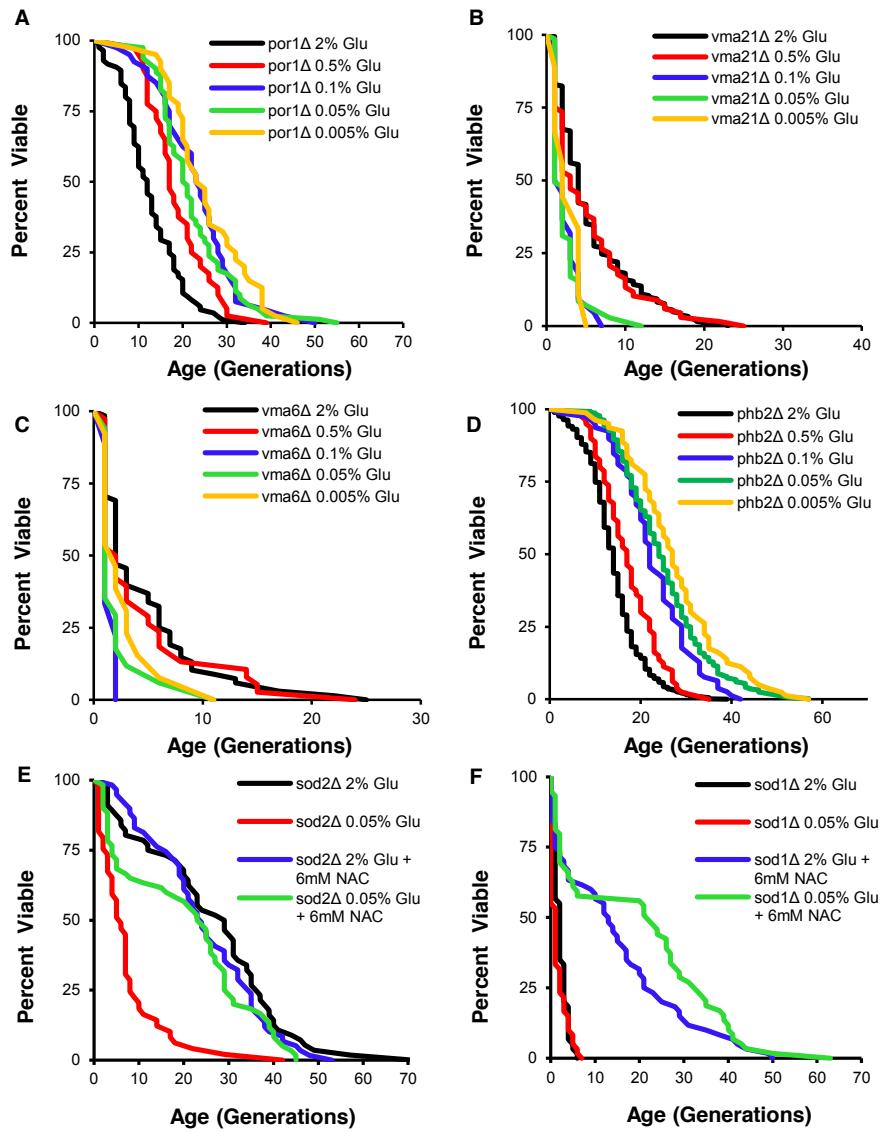
Molecular Function



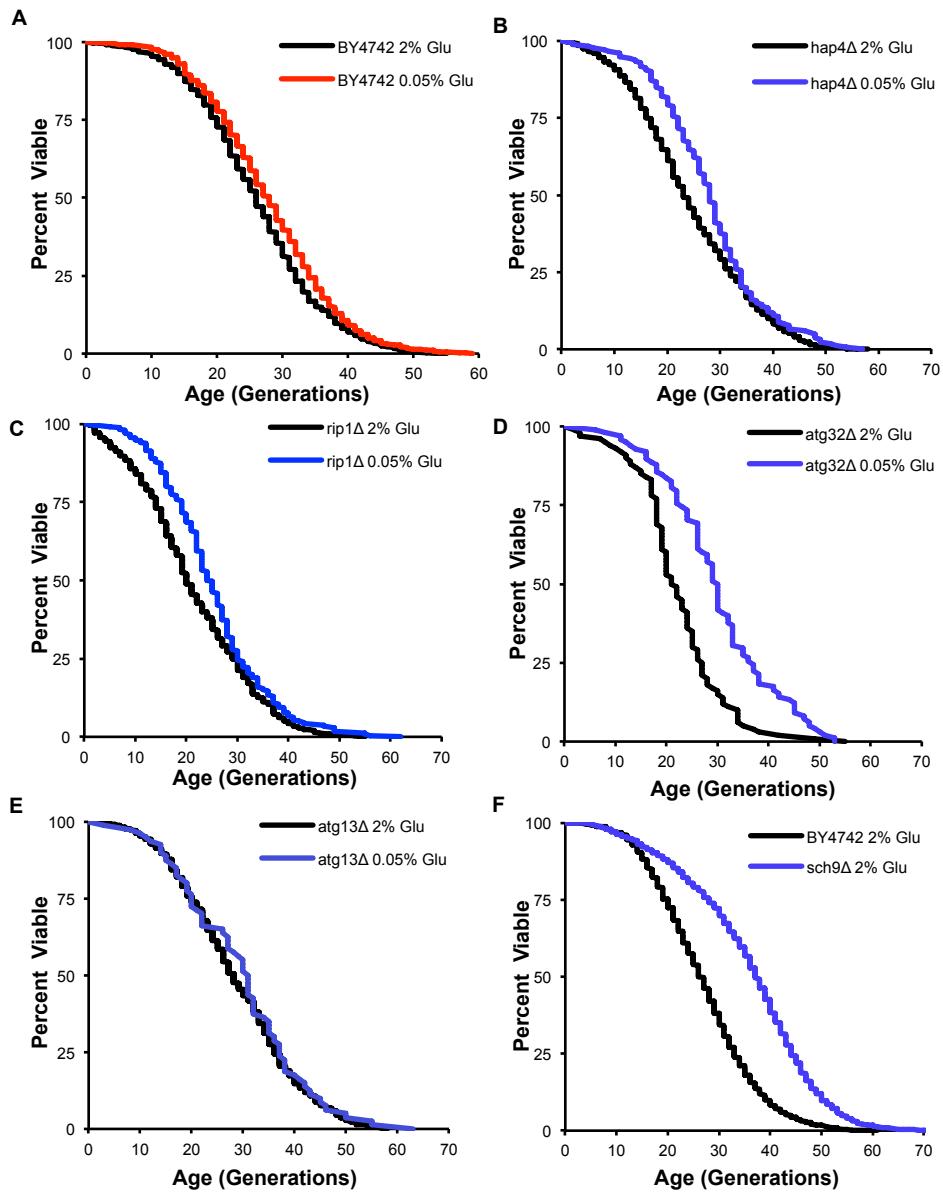
Supplemental Figure 3 – AMIGO Visualization of Molecular Function Groups Significantly Enriched in Mutants with RLS Significantly Decreased by DR. Summary data is presented in Table S6.



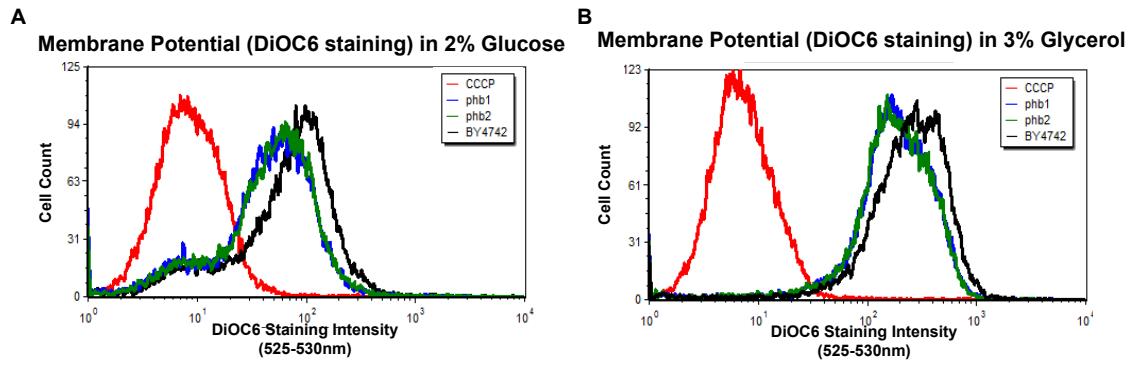
Supplemental Figure 4 – AMIGO Visualization of GO Pathways Significantly Enriched in Mutants with RLS Significantly Increased by DR. Summary data is presented in Table S6.



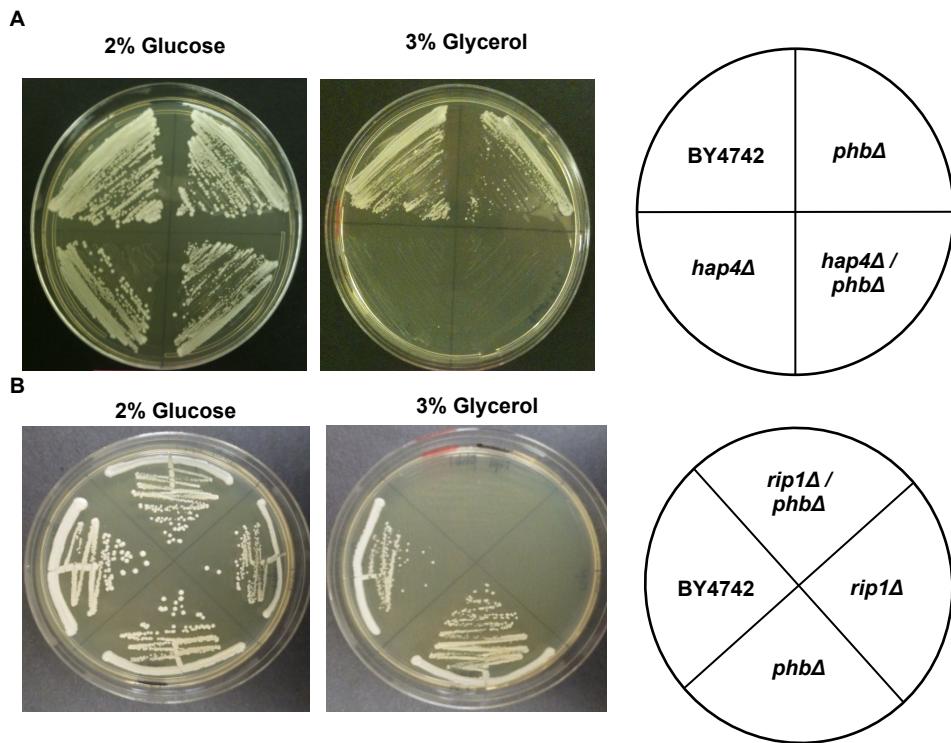
Supplemental Figure 5 – Additional Dose-Response Profiles of Selected Single Gene Mutants on DR. (A) DR increases the RLS of *por1 Δ* cells. (B-C) DR-dosage dependent lifespan reduction of vacuolar mutant *vma6 Δ* and *vma21 Δ* cells. (D) DR-dosage dependent lifespan increase of the prohibitin complex component mutant *phb2 Δ* is identical to that observed for *phb1 Δ* (Fig 2A). (E-F) Treatment of *sod2 Δ* and *sod1 Δ* deficient cells with 6mM N-acetylcysteine increases RLS. Summary data and statistics are presented in Table S1 and S9.



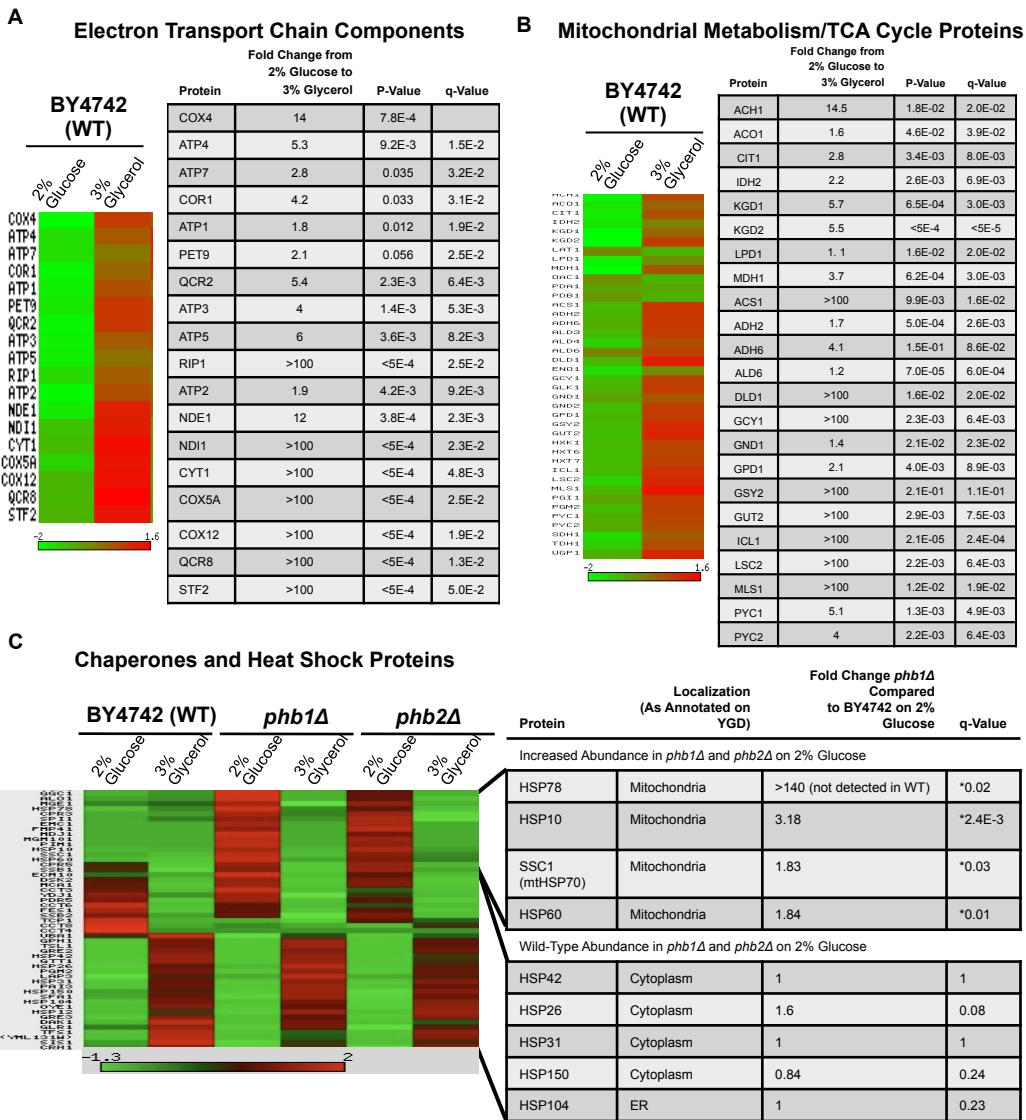
Supplemental Figure 6 – RLS of wild-type and single mutant strains on 2% glucose and DR conditions. RLS of BY4742 (A), *hap4Δ* (B), *rip1Δ* (C), *atg32Δ* (D), *atg13Δ* (E), and cells on 2% glucose (black curve) and 0.05% glucose (blue curve). (F) RLS of BY4742 (black curve) and *sch9Δ* cells (blue curve) on 2% glucose. Summary data and statistics are presented in Table S1.



Supplemental Figure 7 – Prohibitin deficient cells have altered mitochondrial membrane potential.
phb1Δ and *phb2Δ* cells have significantly lower mitochondrial membrane potentials compared to BY4742 in 2% glucose (A) and 3% glycerol (B).

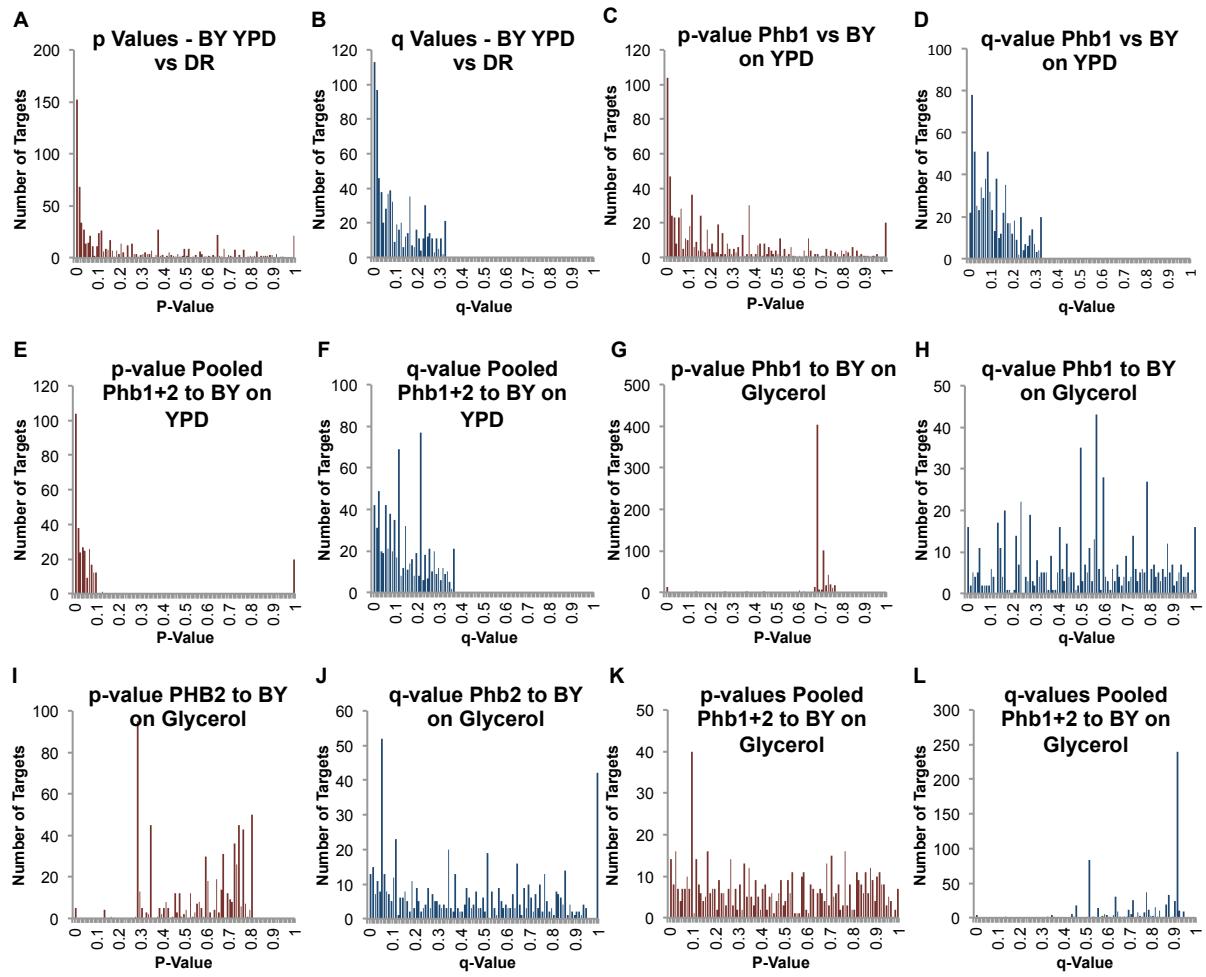


Supplemental Figure 8 – Inhibition of respiration prevents growth of *phbΔ* cells on non-fermentable carbon sources. Deletion of HAP4 (A) or RIP1 (B) in *phbΔ* cells allows for growth on 2% glucose (left panels), but prevents growth on 3% glycerol (center panels).

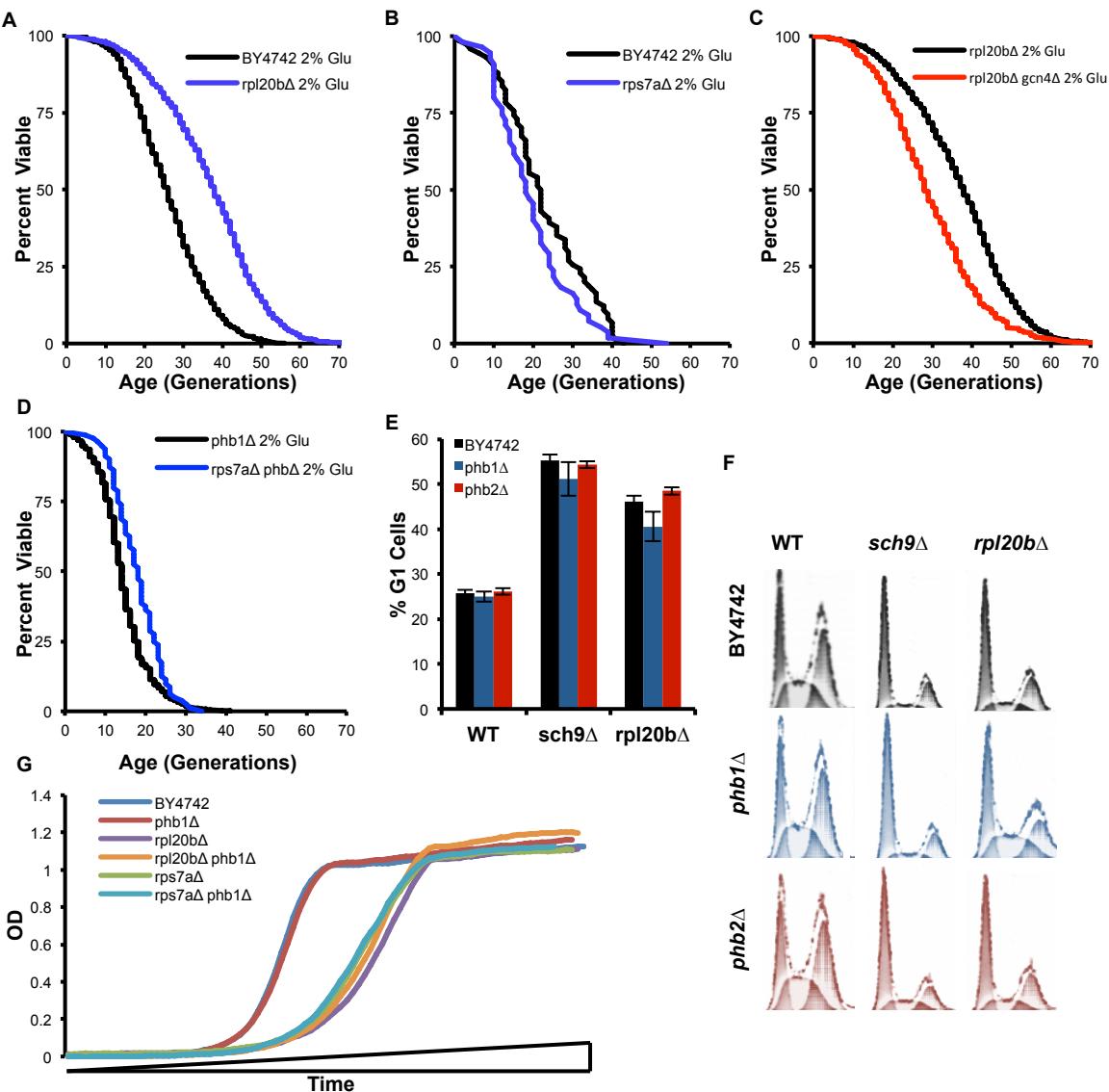


Supplemental Figure 9 - Proteomic analysis reveals expected changes to respiratory proteins on DR as well as revealing the specificity of the induction of the mitochondrial unfolded protein response in *phbΔ* cells.

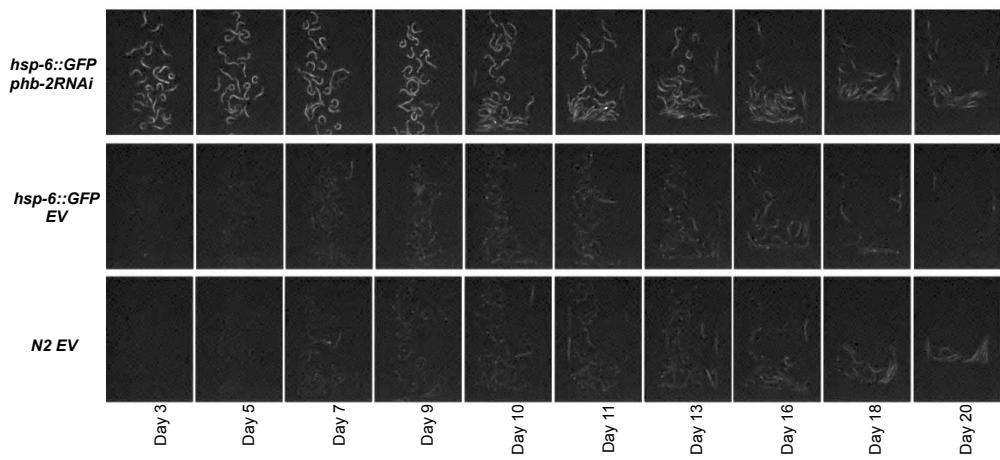
(A) Electron transport chain components show an expected increase in abundance in BY4742, *phb1Δ*, and *phb2Δ* cells grown in 2% glycerol. (B) Krebs cycle and respiratory genes also show an increase in relative abundance in all three cell types grown on 3% glycerol. (C) *phb1Δ* and *phb2Δ* cells show induction of the unfolded protein response (UPR) which is specific to the mitochondrial UPR. Proteins associated with the endoplasmic reticulum (ER) UPR were not increased in abundance in *phb1Δ* and *phb2Δ* cells. Additional data presented in Table S9.



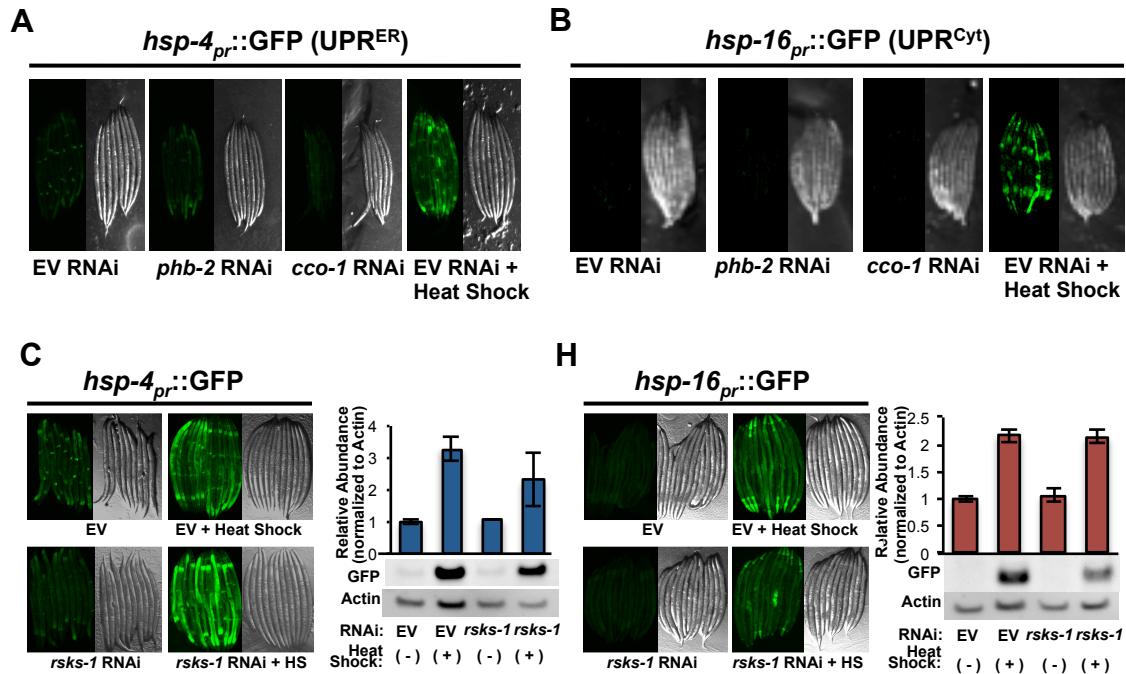
Supplemental Figure 10 – P- and Q-value histograms of proteomic data. (A-F) Histogram distributions of p- and q- values of identified targets compared between *phb1Δ* and/or *phb2Δ* and BY4742 cells show sharp peaks in the low value range typical of significantly different samples. In contrast *phbΔ* cells grown in 3% glycerol are not significantly different than BY4742 cells grown in the same media as demonstrated by the even distribution of the p- and q- values in these comparisons (H-L). Summary data is shown in Table S9.



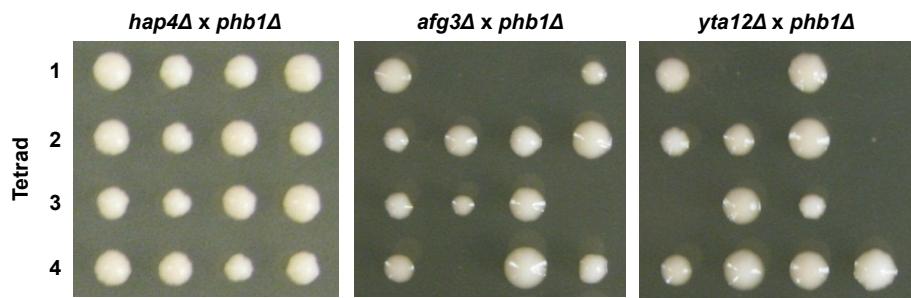
Supplemental Figure 11 – Properties of BY4742 and *phbΔ* cells lacking RPL20B, RPS7A, or SCH9. (A) *rpl20bΔ* cells have an extended RLS compared to BY4742 on 2% glucose. (B) *rps7aΔ* cells do not have an extended RLS compared to BY4742 cells on 2% glucose. (C) Deletion of GCN4 attenuates the extended RLS of *rpl20bΔ* cells. (D) Deletion of RPS7A significantly extends the life span of *phbΔ* cells grown on 2% glucose. (E-F) FACS analysis of Sytox green strained cells shows an increased proportion of cells in G1 phase after deletion of either SCH9 or RPL20B in the BY4742, *phb1Δ*, and *phb2Δ* cells. (G) Deletion of RPL20B or RPS7A causes similar reductions in growth rate in the BY4742 and *phb1Δ* backgrounds. Summary life span data and statistics are presented in Table S1 and S8.



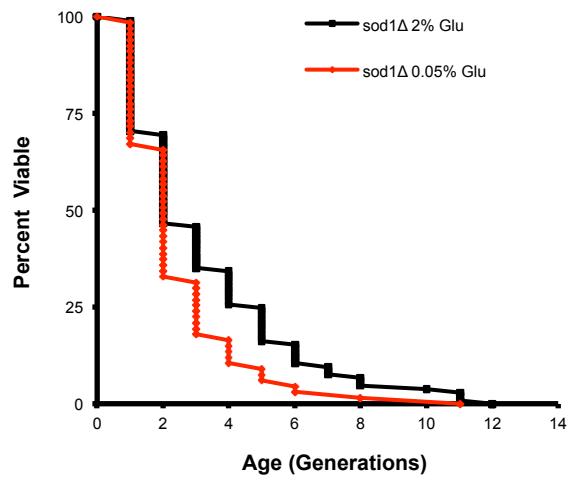
Supplemental Figure 12 – RNAi knockdown of *PHB* in *C. elegans* increases HSP-6 expression throughout their life span. Imaging of *hsp6:gfp* animals treated with *phb-2* RNAi throughout their life spans shows increased expression of *hsp-6* at each time point relative to EV treated controls.



Supplemental Figure 13 – RNAi knockdown of *PHB* in *C. elegans* does not induce the cytoplasmic- or endoplasmic reticulum-associated UPR. (A) *hsp-4_{pr}::GFP*, a reporter for the ER-UPR and (B) *hsp-16_{pr}::GFP*, a reporter for the cytoplasmic UPR, are induced by heat shock, but not RNAi knockdown of *phb-2* or *cco-1*. (C-D) Knockdown of *rsks-1* failed to attenuate induction of the cytoplasmic (C) or ER (D) UPR's.



Supplemental Figure 14 – **Prohibitin deficient cells display synthetic lethal inheritance patterns when crossed to strains lacking AFG3 or YTA12.** Haploid colonies produced after sporulation and microdissection of heterozygous diploid strains lacking PHB1 and HAP4, AFG3, or YTA12. Colonies from each tetrad are shown horizontally.



Supplemental Figure 15 – **DR shortens the RLS of *sod1Δ* cells.** RLS of *sod1Δ* cells on 2% glucose (black line) and 0.05% glucose (red line). Summary life span data is presented in Table S1.

Strain	RLS								Doubling Time				
	2% Glucose	n	0.05% Glucose	n	% Change	Absolute Change	p-value	q-value	2% Glucose	Std. Dev.			
BY4742	25.47	4317	27.32	3727	7.3 (76)	1.9 (74)	7.77E-15	4.27E-15	82.92	1.27			
acb1	27.69	45	36.20	20	30.7 (23)	8.5 (8)	0.00554	0.006	103.39	2.08			
adh3	20.63	110	25.40	90	23.1 (25)	4.8 (32)	0.012	0.012	97.38	16.08			
afg3	25.01	470	20.85	40	-16.6 (133)	-4.2 (133)	0.02	0.018	195.98	11.44			
ahp1	25.56	25	22.90	20	-10.4 (121)	-2.7 (123)	0.33	0.162	86.09	0.76			
aim21	28.96	25	34.40	20	18.8 (34)	5.4 (24)	0.14	0.085	88.25	0.57			
aim29	27.92	25	36.55	20	30.9 (22)	8.6 (7)	0.0035	0.004	103.11	2.01			
aim44	31.08	25	26.10	20	-16.0 (132)	-5.0 (144)	0.177	0.100	87.16	4.05			
aim9	29.84	44	35.47	39	18.9 (33)	5.6 (22)	0.408	0.188	86.74	2.08			
alg12	32.29	185	27.60	20	-14.5 (131)	-4.7 (139)	0.016	0.015	97.63	8.33			
alo1	28.04	45	28.63	39	2.1 (90)	0.6 (90)	0.033	0.028	84.54	1.85			
atg1	28.12	724	22.93	120	-18.5 (139)	-5.2 (145)	1.49E-06	4.32E-06	83.92	1.55			
atg11	27.12	25	23.90	20	-11.9 (124)	-3.2 (128)	0.23	0.122	85.93	0.55			
atg13	28.80	784	29.48	20	2.4 (87)	0.7 (86)	0.39	0.181	85.80	1.36			
atg32	21.96	100	31.09	98	41.6 (14)	9.1 (6)	5.71E-08	2.07E-07	87.44	1.74			
atg8	30.75	130	24.80	120	-19.3 (140)	-6.0 (150)	7.15E-06	1.60E-05	88.92	1.83			
atp1	7.01	102	11.27	78	60.7 (5)	4.3 (38)	9.63E-08	3.10E-07	139.35	6.64			
atp11	28.87	30	24.70	20	-14.4 (129)	-4.2 (134)	0.106	0.068	135.63	7.73			
atp5	22.20	55	25.50	50	14.7 (44)	3.3 (52)	0.719	0.274	101.66	2.80			
bem4	19.34	44	12.57	35	-35.0 (155)	-6.8 (156)	0.0001	0.000166	100.89	1.02			
bre5	27.45	115	26.75	40	-2.6 (101)	-0.7 (101)	0.946	0.335	93.23	0.86			
caf20	28.44	385	27.50	120	-3.3 (105)	-0.9 (106)	0.197	0.108	92.76	2.43			
ccp1	24.68	25	28.60	20	15.9 (142)	3.9 (39)	0.298	0.150	87.19	2.60			
coq2	25.27	85	28.86	50	14.2 (47)	3.6 (44)	0.073	0.052	94.67	3.30			
coq3	21.09	35	28.45	20	34.9 (19)	7.4 (15)	0.014	0.013538	107.68	15.51			
coq4	17.53	45	25.97	30	48.1 (11)	8.4 (9)	1.43E-05	2.96E-05	147.66	11.61			
ctt1	24.91	43	25.10	20	0.8 (93)	0.2 (93)	0.864	0.318	90.41	0.82			
cup2	30.32	45	28.65	40	-5.5 (113)	-1.7 (118)	0.54	0.225	86.48	0.57			
cyt2	17.89	46	25.30	20	41.4 (15)	7.4 (14)	0.005	0.005473	113.64	4.82			
dbp3	31.38	125	25.90	20	-17.5 (135)	-5.5 (148)	0.026	0.022852	118.25	6.34			
dlt1	31.26	144	13.05	40	-58.2 (162)	-18.2 (166)	1.53E-12	8.07E-12	93.25	1.98			
dot5	32.88	24	33.90	20	3.1 (86)	1.0 (84)	0.486	0.211	87.88	2.25			
erg6	28.42	50	19.50	20	-31.4 (154)	-8.9 (160)	0.0013	0.001754	98.37	10.72			
est3	12.40	34	13.00	30	4.8 (83)	0.6 (89)	0.214	0.115	138.21	12.20			
exo1	23.72	25	23.90	20	0.8 (94)	0.2 (94)	0.936	0.334	95.44	0.94			
fov1	32.98	4318	39.17	1531	18.8 (35)	6.2 (19)	6.63E-49	7.69E-48	89.29	2.15			
fzo1	30.00	24	33.54	98	11.8 (56)	3.5 (46)	0.00033	0.000504	135.12	26.86			
gad1	30.68	25	24.25	20	-21.0 (144)	-6.4 (154)	0.046	0.03606	99.63	6.07			
gcn2	25.84	895	28.86	101	11.7 (58)	3.0 (57)	0.008	0.008342	84.00	0.98			
gcn20	25.97	60	28.00	40	7.8 (73)	2.0 (73)	0.249	0.128966	110.35	6.02			
gcn3	25.03	60	27.80	40	11.1 (59)	2.8 (59)	0.114	0.071881	87.29	2.17			
gcn4	27.64	1825	27.02	179	-2.2 (98)	-0.6 (99)	0.456	0.205055	92.71	4.39			
gef1	26.24	25	26.40	20	0.6 (95)	0.2 (95)	0.872	0.318137	91.93	2.94			
gpx1	20.12	25	27.25	20	35.4 (17)	7.1 (17)	0.056	0.041647	103.51	4.84			
gpx2	26.97	29	27.60	20	2.4 (89)	0.6 (88)	0.714	0.274397	91.69	0.34			
gtt2	29.20	25	32.30	20	10.6 (61)	3.1 (56)	0.471	0.210171	88.05	0.67			
hac1	29.15	543	27.55	40	-5.5 (112)	-1.6 (116)	0.374	0.177831	90.70	1.78			
hap4	24.39	1259	28.13	180	15.4 (43)	3.7 (40)	4.34E-06	1.05E-05	95.75	0.91			
hcs1	25.92	25	27.05	20	4.4 (85)	1.1 (83)	0.766	0.286576	96.43	3.20			
hmo1	19.07	761	19.28	40	1.1 (92)	0.2 (92)	0.584	0.239852	129.45	3.41			
hmx1	25.54	44	28.68	39	12.3 (54)	3.1 (54)	0.657	0.264666	95.94	4.06			
hop1	25.72	45	24.00	39	-6.9 (116)	-1.7 (119)	0.48	0.210941	93.84	5.85			
hor7	34.33	43	28.10	20	-18.1 (137)	-6.2 (152)	0.053	0.039928	101.83	12.44			
hsp104	31.93	45	16.40	20	-48.6 (158)	-15.5 (165)	1.64E-06	4.32E-06	111.47	10.53			
hst4	22.55	145	24.65	20	9.3 (66)	2.1 (70)	0.134	0.081823	108.44	3.44			
hxk2	32.62	605	24.40	20	-25.2 (149)	-8.2 (159)	0.0024	0.003027	108.03	12.04			
hyr1	22.45	85	20.24	80	-9.8 (120)	-2.2 (121)	0.095	0.05408	122.66	10.59			
idh1	32.84	304	33.20	20	1.1 (91)	0.4 (91)	0.997	0.384803	117.66	26.28			
ifm1	23.92	24	27.25	20	10.9 (148)	3.3 (50)	0.084	0.058009	101.39	7.18			
inh1	29.05	84	31.50	80	8.4 (71)	2.5 (62)	0.104	0.067032	91.42	0.83			
inn1	26.26	85	29.60	20	12.7 (51)	3.3 (49)	0.172	0.079819	95.24	2.75			
inp51	30.88	350	33.30	20	7.8 (74)	2.4 (63)	0.515	0.218063	86.18	2.71			
inp53	31.72	235	31.48	40	-0.8 (96)	-0.2 (96)	0.731	0.277154	86.77	1.23			
ire1	26.34	145	23.45	40	-11.0 (123)	-2.9 (125)	0.037	0.03023	93.61	4.16			
isw2	32.03	345	27.82	80	-13.1 (125)	-4.2 (135)	0.168	0.097455	89.47	1.56			
lat1	24.46	175	26.72	80	9.7 (65)	2.4 (67)	0.168	0.096096	88.24	0.92			
mcr1	25.40	25	29.95	20	17.9 (36)	4.6 (34)	0.184	0.020631	85.87	1.21			
mdm1	33.56	85	26.18	80	-22.0 (147)	-7.4 (158)	1.57E-06	4.32E-06	98.57	4.55			
mfel1	31.44	25	37.70	20	16.9 (30)	6.2 (18)	0.037	0.03023	141.09	3.32			
mgm1	25.05	85	28.05	60	12.0 (55)	3.0 (58)	0.002	0.002578	148.58	15.53			
mrr1	27.31	64	28.58	60	4.7 (84)	1.3 (82)	0.714	0.274397	141.10	24.88			
mms22	8.52	25	4.40	20	-48.4 (157)	-4.1 (132)	0.00307	0.00371	200.23	15.80			
mre11	8.04	25	12.30	20	53.0 (8)	4.3 (37)	0.004	0.004029	147.19	4.78			
mrpl4	24.58	125	37.15	20	51.1 (10)	12.6 (2)	0.01	0.010002	117.75	3.48			
mth1	27.07	55	28.75	20	6.2 (81)	1.7 (80)	0.453	0.205055	85.21	11.24			
ncr1	24.89	35	28.53	30	14.7 (45)	3.6 (43)	0.059	0.042782	100.09	7.45			
nde1	28.27	90	21.72	78	-23.2 (148)	-6.5 (155)	1.38E-05	2.96E-05	90.96	2.07			
nd11	31.19	85	19.28	80	-38.2 (156)	-11.9 (162)	6.80E-14	3.94E-13	99.24	5.54			
nen1	18.25	85	19.89	80	9.0 (69)	1.6 (81)	0.694	0.273865	93.17	2.83			
nha1	21.40	25	19.85	20	-7.2 (118)	-1.6 (115)	0.757	0.285148	94.68	0.59			
nhx1	12.64	45	25.57	60	102.2 (2)	12.9 (1)	9.13E-10	4.07E-09	131.99	9.38			
nhp170	9.70	30	12.10	20	24.7 (24)	2.4 (64)	0.022	0.019941	105.96	1.32			
nup84	8.80	45	7.63	39	-13.3 (126)	-1.2 (110)	0.679	0.269781	174.14	57.41			
pda1	15.86	107	21	40	90	34.9 (18)	5.5 (23)	0.001	0.00166	188.94	5.64		
pdb1	13.09	54	20	30	50	55.1 (7)	7.2 (16)	4.40E-09	1.82E-08	108.14	1.97		
pdx1	18.97	54	20	27.3	50	9.3 (67)	1.8 (77)	0.475	0.210338	88.91	1.82		
pex13	22.48	40	16	70	20	-25.7 (150)	-5.8 (149)	0.003	0.003703	99.39	0.90		
pex19	33.75	64	27	65	20								

Gene Name	Annotated Function	% Change	p-value	q-value
por1	Mitochondrial outer membrane protein	103.79	4.39E-17	4.24E-16
nhx1	Vacuolar ion exchanger	102.20	9.13E-10	4.07E-09
phb2	Mitochondrial membrane chaperone	80.75	1.39E-78	2.69E-77
phb1	Mitochondrial membrane chaperone	76.02	4.26E-85	1.24E-83
atp1	Mitochondrial ATP synthase	60.74	9.63E-08	3.10E-07
tsa1	Thioredoxin peroxidase	59.63	2.66E-06	6.71E-06
pdb1	E1 beta subunit of pyruvate dehydrogenase complex	55.10	4.40E-09	1.82E-08
mre11	DNA double strand break repair	52.99	0.0034	0.004025
rad51	DNA double strand break repair	52.39	1.50E-04	2.42E-04
mrp14	Mitochondrial ribosomal subunit	51.11	0.01	0.010002
cog4	Component of a mitochondrial ubiquinone-synthesizing complex	48.10	1.43E-05	2.96E-05
tom71	Recognition and import of mitochondrial directed proteins	47.10	0.005	0.005473
tom70	Recognition and import of mitochondrial directed proteins	42.65	4.45E-05	8.33E-05
atg32	Mitochondrial outer membrane protein required to initiate mitophagy	41.56	5.71E-08	2.07E-07
cyt2	Cytochrome C1 heme lyase	41.41	0.005	0.005473
rad55	DNA double strand break repair	41.13	0.048	0.037126
gpx1	Phospholipid hydroperoxide glutathione peroxidase	35.44	0.056	0.041647
pda1	E1 alpha subunit of pyruvate dehydrogenase complex	34.93	0.0001	0.000166
coq3	O-methyltransferase in ubiquinone biosynthesis	34.93	0.014	0.013535
pos5	Mitochondrial NADH kinase	34.65	1.59E-05	3.18E-05
vps3	Sorting and processing of soluble vacuolar proteins	31.95	0.008	0.008142
aim29	Unknown function	30.91	0.0035	0.004061
acb1	Acyl-CoA binding protein	30.74	0.0054	0.005951
nup170	Subunit of nuclear pore complex	24.74	0.022	0.019941
adh3	Mitochondrial alcohol dehydrogenase	23.10	0.012	0.011798
rpn4	Transcription factor which regulates proteasome genes	23.00	0.0005	0.000725
rps17a	Cytoplasmic ribosomal subunit	23.05	0.005	0.005473
mef1	Mitochondrial elongation factor	19.91	0.037	0.03023
stv1	Vacuolar ATPase subunit	19.42	0.058	0.042589
ung1	Uracil-DNA glycosylase	18.95	0.024	0.021419
fob1	Required for replication fork blocking	18.76	6.63E-49	7.69E-48
rip1	Rieske iron-sulfur protein of the mitochondrial cytochrome bc1 complex	17.02	5.17E-06	1.20E-05
sgs1	Nucleolar DNA helicase of the RecQ family	16.56	0.05	0.038164
hap4	Transcriptional activator of respiratory genes	15.35	4.34E-06	1.05E-05
ncr1	Vacuolar protein involved in sphingolipid metabolism	14.66	0.059	0.042782
rpl31a	Cytoplasmic ribosomal subunit	14.38	6.04E-05	6.04E-05
rpl20b	Cytoplasmic ribosomal subunit	13.88	0.0004	0.000595
mgm1	Mitochondrial GTPase	11.99	0.002	0.002578
fzo1	Involved in mitochondrial outer membrane tethering and fusion	11.79	0.00033	0.000504
sgf73	Involved in preinitiation complex assembly at promoters	11.70	5.23E-17	4.33E-16
gcn2	Protein kinase	11.70	0.008	0.008142
whi5	Repressor of G1 transcription	6.54	0.075	0.052418
alo1	D-Arabinono-1,4-lactone oxidase	2.11	0.033	0.027743
tor1	PIK-related protein kinase	-6.88	0.002	0.002578
ire1	Transmembrane protein, mediates the unfolded protein response (UPR)	-10.96	0.037	0.03023
ybr238	Mitochondrial membrane protein	-14.48	0.0009	0.001243
alg12	Alpha-1,6-mannosyltransferase	-14.52	0.016	0.01497
afg3	Mitochondrial inner membrane m-AAA protease	-16.63	0.02	0.018416
vcx1	Vacuolar membrane antiporter	-17.08	0.015	0.014264
dbp3	Putative ATP-dependent RNA helicase	-17.47	0.026	0.022852
pex19	Protein chaperone	-18.07	0.028	0.024243
hor7	Unknown function	-18.14	0.053	0.039928
vps4	AAA-ATPase involved in multivesicular body (MVB) protein sorting	-18.42	0.038	0.030616
atg1	Protein ser/thr kinase required for vesicle formation in autophagy	-18.47	1.49E-06	4.32E-06
atg8	Component of autophagosomes	-19.34	7.15E-06	1.60E-05
sch9	AGC family protein kinase	-19.43	0.0001	0.000166
rad23	DNA damage repair	-19.79	0.044	0.034964
rgd1	GTPase activating protein	-20.71	0.031	0.026445
gad1	Glutamate decarboxylase	-20.96	0.046	0.03606
ptc6	Mitochondrial type 2C protein phosphatase	-21.37	2.85E-05	5.51E-05
sir2	Conserved NAD+ dependent histone deacetylase of the Sirtuin family	-21.68	9.77E-42	9.45E-41
mdm1	Intermediate filament protein	-22.02	1.57E-06	4.32E-06
nde1	Mitochondrial external NADH dehydrogenase	-23.17	1.38E-05	2.96E-05
hox2	Hexokinase isoenzyme 2	-25.21	0.0024	0.003027
pex13	Integral peroxisomal membrane protein	-25.70	0.003	0.003703
sod1	Cytosolic copper-zinc superoxide dismutase	-26.44	0.063	0.045118
stf2	Protein involved in regulation of the mitochondrial F1FO-ATP synthase	-27.18	0.0002	0.000314
rad6	Ubiquitin-conjugating enzyme (E2)	-30.23	0.0008	0.001132
erg6	Delta(24)-sterol C-methyltransferase	-31.39	0.0013	0.001754
bem4	Protein involved in establishment of cell polarity and bud emergence	-35.00	0.0001	0.000166
ndi1	NADH:ubiquinone oxidoreductase	-38.20	6.80E-14	3.94E-13
mms22	Subunit of an E3 ubiquitin ligase complex involved in replication repair	-48.36	0.00307	0.00371
hsp104	Heat shock protein	-48.64	1.64E-06	4.32E-06
vma2	Subunit of vacuolar ATPase	-48.70	0.0001	0.000166
put3	Transcriptional activator of proline utilization genes	-48.88	1.45E-06	4.32E-06
vma6	Subunit of vacuolar ATPase	-56.32	0.007	0.007383
dlt1	Unknown function	-58.25	1.53E-12	8.07E-12
pmr1	Ca2+/Mn2+ P-type ATPase	-59.18	3.38E-54	4.90E-53
vma21	Subunit of vacuolar ATPase	-62.67	3.05E-10	1.47E-09
vma13	Subunit of vacuolar ATPase	-65.90	1.04E-08	4.02E-08
vma5	Subunit of vacuolar ATPase	-77.68	6.76E-08	2.31E-07
sod2	Mitochondrial manganese superoxide dismutase	-79.45	2.63E-85	1.24E-83

Supplemental Table 2 – Life spans of strains with statistically significant difference in RLS between 2% glucose and 0.05% glucose

Category	Gene Ontology (GO)Term	GO Term ID	Count	Percent of Genes	DR vs Mutant Set	p-Value	Benjamini -test value	Fold Enrichment:		Fold Enrichment in DR	Fold Enrichment in Total Gene Set
								Negative Response to	Response to		
GOTERM CC FAT	organelle membrane	GO:0031090	17	44.7	1.48	4.00E-06	4.40E-04	VPH1, SCH9, YME1, POR1, YBR238C, ERG6, TOM6, AFG3, PMC1, ALO1, ATG8, STF1, ATP1, STF2, TOR1, PEX19, VMA21, PEX13, UGO1, MGM1, ATP5, FZO1, PMT1, TOM70, SPF1, STV1, VTC4, YLH47, NCR1, COQ4, COQ3, VMA2, COO2, VMA5, ND11, MMR1, VMA6, PHB2, MCR1, PHB1, INH1, CYT2, PMR1, ALG12, VMA13, RIP1		3.38	2.28
GOTERM BP FAT	age-dependent response to oxidative stress	GO:0001306	4	10.5	4.33	1.20E-05	1.80E-03	SCH9, SOD1, SOD2, HSP104		77.30	17.84
GOTERM BP FAT	age-dependent general metabolic decline	GO:0007571	4	10.5	4.33	1.20E-05	1.80E-03	SCH9, SOD1, SOD2, HSP104		77.30	17.84
GOTERM BP FAT	cell aging	GO:0007569	7	18.4	2.02	4.90E-06	2.30E-03	SCH9, YME1, FOB1, HXK2, SOD1, PNC1, SOD2, ND11, NDE1, PHB2, SGS1, RTG2, SIR3, PHB1, HSP104		14.80	7.32
GOTERM BP FAT	chronological cell aging	GO:0001300	5	13.2	3.61	2.10E-05	2.50E-03	SCH9, YME1, ND11, NDE1, SOD1, SOD2		28.18	7.80
GOTERM BP FAT	aging	GO:0007568	7	18.4	2.02	1.10E-05	2.70E-03	SCH9, YME1, FOB1, HXK2, SOD1, PNC1, SOD2, ND11, NDE1, PHB2, SGS1, RTG2, SIR3, PHB1, HSP104		12.80	6.33
GOTERM MF FAT	cation-transporting ATPase activity	GO:0019829	5	13.2	2.32	3.30E-05	4.20E-03	VPH1, VMA2, VMA5, ATP1, VMA6, STV1, PMR1, ATP5, PMC1, VMA13		25.03	10.78
GOTERM CC FAT	vacuolar membrane	GO:0005774	7	18.4	2.39	1.70E-04	4.80E-03	VPH1, SCH9, ATG8, VMA2, VMA5, TOR1, VMA6, STV1, VTC4, NCR1, PMC1, VMA13		7.86	3.29
GOTERM CC FAT	vacuolar part	GO:0044437	7	18.4	2.39	2.40E-04	5.20E-03	VPH1, SCH9, ATG8, VMA2, VMA5, TOR1, VMA6, STV1, VTC4, NCR1, PMC1, VMA13		7.44	3.12
GOTERM CC FAT	proton-transporting two-sector ATPase complex	GO:0016469	5	13.2	1.86	9.80E-05	5.40E-03	VPH1, VMA2, VMA5, STF1, ATP1, STF2, VMA6, STV1, INH1, ATP5, VMA13		19.34	10.40
GOTERM CC FAT	vacuolar proton-transporting V-type ATPase complex	GO:0033176	4	10.5	2.73	1.60E-04	6.00E-03	VPH1, VMA2, VMA5, VMA6, STV1, VMA13		34.81	12.76
GOTERM CC FAT	proton-transporting V-type ATPase complex	GO:0016471	4	10.5	2.73	1.60E-04	6.00E-03	VCX1, VMA2, VMA5, VMA6, SOD1, VMA13		34.81	12.76
GOTERM MF FAT	ATPase activity	GO:0016887	9	23.7	1.61	5.50E-04	9.80E-03	YME1, VPH1, HCS1, AFG3, PMC1, ATP1, ISW2, ATP5, HSP104, EST3, SPF1, STV1, RAD57, RAD55, VPS4, RAD50, RAD51, VMA2, VMA5, VMA6, TIF1, SGS1, DBP3, TIF2, PMR1, GCN20, VMA13		4.38	2.72
GOTERM MF FAT	nucleoside binding	GO:0001882	14	36.8	2.03	5.30E-04	1.10E-02	SCH9, AFG3, HXK2, VPS4, RAD6, ATG1, NDE1, VMA5, ND11, TOR1, IRE1, DBP3, PMR1, HSP104		2.70	1.33
GOTERM MF FAT	ATPase activity, coupled to transmembrane movement of ions	GO:0042625	5	13.2	2.11	1.80E-04	1.10E-02	VMA2, VMA5, VMA6, PMR1, VMA13		16.48	7.81
GOTERM MF FAT	proton-transporting ATPase activity, rotational mechanism	GO:0046961	4	10.5	2.32	5.30E-04	1.30E-02	VMA2, VMA5, VMA6, VMA13		23.51	10.12
GOTERM MF FAT	purine nucleoside binding	GO:0001883	14	36.8	2.03	5.00E-04	1.50E-02	YME1, SCH9, HCS1, AFG3, ALO1, RAD6, PMC1, ISW2, ATP1, POS5, NDE1, TOR1, IRE1, PKH2, GCN2, HSP104, SPF1, RAD57, HXK2, RAD55, VPS4, SAM1, RAD50, ATG1, RAD51, ND11, VMA5, SGS1, TIF1, TIF2, DBP3, PMR1, GCN20		2.72	1.34
GOTERM MF FAT	hydrolase activity, acting on acid anhydrides, catalyzing transmembrane movement of substances	GO:0016820	5	13.2	2.11	1.00E-03	1.60E-02	VMA2, VMA5, VMA6, PMR1, VMA13		10.56	5.00
GOTERM MF FAT	ATPase activity, coupled to transmembrane movement of substances	GO:0042626	5	13.2	2.11	1.00E-03	1.60E-02	VMA2, VMA5, VMA6, PMR1, VMA13		10.56	5.00
GOTERM MF FAT	inorganic cation transmembrane transporter activity	GO:0015077	6	15.8	1.69	1.30E-03	1.60E-02	VMA2, VMA5, VMA6, VMA13		7.61	4.51
GOTERM MF FAT	ATPase activity, coupled to movement of substances	GO:0043492	5	13.2	2.11	1.30E-03	1.70E-02	VMA2, VMA5, VMA6, PMR1, VMA13		9.94	4.71
GOTERM BP FAT	nucleoside triphosphate biosynthetic process	GO:0009145	5	13.2	1.97	5.10E-04	1.80E-02	VMA2, VMA5, VMA6, PMR1, VMA13		13.80	7.01
GOTERM BP FAT	ribonucleoside triphosphate metabolic process	GO:0009205	5	13.2	1.97	4.70E-04	1.80E-02	VPH1, VMA2, VMA5, ATP1, VMA6, SPF1, STV1, PMR1, ATP5, PMC1, VMA13		13.53	6.87
GOTERM BP FAT	ribonucleoside triphosphate biosynthetic process	GO:0009201	5	13.2	1.97	4.40E-04	1.80E-02	VPH1, VMA2, VMA5, ATP1, VMA6, SPF1, STV1, PMR1, ATP5, PMC1, VMA13		13.26	6.73

Supplemental Table 3 – GO Terms significantly enriched in single gene mutant set for decreased lifespan on DR (1 of 3)

Category	Gene Ontology (GO) Term		GO Term ID	Percent Count of Genes	Fold Enrichment: Negative Response to DR vs Mutant Set			Benjamani-test Value	Genes	Fold Enrichment in Negative Response to DR	Fold Enrichment in Total Gene Set
	Term	Term Description			p-Value	Negative Response to DR	Total Gene Set				
GOTERM_B_P_FAT	phosphorus metabolic process	GO:0006793	9	23.7	1.86	8.00E-04	1.80E-02	SCH9, VMA2, VMA5, NDI1, VMA6, IRE1, PTC6, ATG1, VMA13		4.21	2.27
GOTERM_B_P_FAT	cellular cation homeostasis	GO:0030003	6	15.8	1.63	9.30E-04	1.90E-02	VCX1, VMA2, VMA5, VMA6, SOD1, VMA13		7.52	4.62
GOTERM_B_P_FAT	purine nucleoside triphosphate metabolic process	GO:0009144	5	13.2	1.97	4.10E-04	1.90E-02	VPH1, VMA2, VMA5, ATP1, VMA6, SPF1, STV1, PMR1, ATP5, PMC1, VMA13		13.53	6.87
GOTERM_B_P_FAT	purine ribonucleoside triphosphate metabolic process	GO:0009205	5	13.2	1.97	4.10E-04	1.90E-02	VMA2, VMA5, VMA6, PMR1, VMA13		13.53	6.87
GOTERM_M_F_FAT	purine nucleotide binding	GO:0017076	14	36.8	1.76	1.70E-03	1.90E-02	SCH9, AFG3, HXK2, VPS4, RAD6, ATG1, NDE1, VMA5, NDI1, TOR1, IRE1, DBP3, PMR1, HSP104		2.40	1.37
GOTERM_B_P_FAT	chemical homeostasis	GO:0048878	7	18.4	1.69	9.00E-04	1.90E-02	VCX1, VMA2, VMA5, VMA6, PMR1, SOD1, VMA13		5.85	3.47
GOTERM_M_F_FAT	primary active transmembrane transporter activity	GO:0015399	5	13.2	1.94	1.80E-03	1.90E-02	VPH1, VMA2, VMA5, ATP1, TOM70, VMA6, SPF1, STV1, PMR1, ATP5, PMC1, VMA13		9.01	4.66
GOTERM_M_F_FAT	P-P bond-hydrolysis-driven transmembrane transporter activity	GO:0015405	5	13.2	1.94	1.80E-03	1.90E-02	VPH1, VMA2, VMA5, ATP1, TOM70, VMA6, SPF1, STV1, PMR1, ATP5, PMC1, VMA13		9.01	4.66
GOTERM_B_P_FAT	ion homeostasis	GO:0050801	7	18.4	1.69	8.70E-04	1.90E-02	VCX1, VMA2, VMA5, VMA6, PMR1, SOD1, VMA13		5.88	3.49
GOTERM_B_P_FAT	regulation of cellular pH	GO:0030641	4	10.5	2.17	7.90E-04	1.90E-02	VPH1, VMA2, VMA5, NHX1, VMA6, STV1, VPS3, VMA13		20.81	9.61
GOTERM_B_P_FAT	regulation of intracellular pH	GO:0051453	4	10.5	2.17	7.90E-04	1.90E-02	VMA2, VMA5, VMA6, VMA13		20.81	9.61
GOTERM_B_P_FAT	purine nucleoside triphosphate biosynthetic process	GO:0009145	5	13.2	1.97	3.80E-04	1.90E-02	VMA2, VMA5, VMA6, PMR1, VMA13		13.80	7.01
GOTERM_B_P_FAT	purine ribonucleoside triphosphate biosynthetic process	GO:0009206	5	13.2	1.97	3.80E-04	1.90E-02	VMA2, VMA5, VMA6, PMR1, VMA13		13.80	7.01
GOTERM_B_P_FAT	cellular response to stress	GO:0033554	13	34.2	1.56	3.40E-04	1.90E-02	SCH9, RGD1, MMS22, RAD6, ATG1, ATG8, RAD23, STF2, TOR1, IRE1, PTC6, GAD1, HSP104		3.13	2.00
GOTERM_M_F_FAT	adenyl nucleotide binding	GO:0030554	14	36.8	2.03	4.70E-04	2.00E-02	SCH9, AFG3, HXK2, VPS4, RAD6, ATG1, NDE1, VMA6, NDI1, TOR1, IRE1, DBP3, PMR1, HSP104		2.73	1.34
GOTERM_B_P_FAT	oxidative phosphorylation	GO:0006119	5	13.2	2.17	7.70E-04	2.00E-02	VMA2, VMA5, NDI1, VMA6, VMA13		11.46	5.29
GOTERM_B_P_FAT	nucleoside triphosphate metabolic process	GO:0009205	5	13.2	1.97	7.70E-04	2.00E-02	VMA2, VMA5, VMA6, PMR1, VMA13		13.53	6.87
GOTERM_B_P_FAT	phosphorylation	GO:0006119	8	21.1	2.17	6.20E-04	2.00E-02	VPH1, VMA2, VMA5, NDI1, ATP1, VMA6, STV1, ATP5, VMA13, RIP1		11.46	5.29
GOTERM_B_P_FAT	phosphate metabolic process	GO:0006796	9	23.7	1.95	7.20E-04	2.00E-02	SCH9, VPH1, INM1, STV1, VTC4, ATG1, VMA2, NDI1, ATP1, VMA5, INP51, VMA6, IRE1, PTC6, INP53, GCN2, PKH2, ATP5, RIP1, VMA13		4.29	2.20
GOTERM_B_P_FAT	ATP metabolic process	GO:0046034	5	13.2	1.97	3.20E-04	2.10E-02	VPH1, VMA2, VMA5, ATP1, VMA6, SPF1, STV1, PMR1, ATP5, PMC1, VMA13		14.39	7.31
GOTERM_B_P_FAT	cation homeostasis	GO:0055080	6	15.8	1.63	1.10E-03	2.10E-02	VPH1, NHA1, HMX1, NHX1, SPF1, STV1, VPS3, SOD1, PMC1, VCX1, VMA2, VMA5, VMA6, TIS11, GEF1, VMA13		7.25	4.46
GOTERM_B_P_FAT	vacuolar acidification	GO:0007035	4	10.5	2.17	7.00E-04	2.10E-02	VPH1, VMA2, VMA5, NHX1, VMA6, STV1, VPS3, VMA13		21.64	9.99
GOTERM_B_P_FAT	intracellular pH reduction	GO:0051452	4	10.5	2.17	7.00E-04	2.10E-02	VPH1, VMA2, VMA5, NHX1, VMA6, STV1, VPS3, VMA13		21.64	9.99
GOTERM_B_P_FAT	pH reduction	GO:0045851	4	10.5	2.17	7.00E-04	2.10E-02	VPH1, VMA2, VMA5, NHX1, VMA6, STV1, VPS3, VMA13		21.64	9.99
GOTERM_B_P_FAT	regulation of pH	GO:0006885	4	10.5	2.17	1.20E-03	2.20E-02	VPH1, VMA2, VMA5, NHX1, VMA6, STV1, VPS3, VMA13		18.04	8.32

Supplemental Table 4 – GO Terms significantly enriched in single gene mutant set for decreased lifespan on DR (2 of 3)

Category	Gene Ontology (GO) Term	GO Term ID	Count	Percent of Genes	Fold Enrichment: Negative Response to DR vs Mutant Set			Genes	Fold Enrichment in Negative Response to DR	Fold Enrichment in Response to DR	Total Gene Set
					p-Value	Benjamini-test Value					
GOTERM_BP_FAT	ATP synthesis coupled proton transport	GO:0015986	4	10.5	2.17	1.20E-03	2.20E-02	VPH1, VMA2, VMA5, ATP1, VMA6, STV1, ATP5, VMA13	18.04	8.32	
GOTERM_BP_FAT	energy coupled proton transport, down electrochemical gradient	GO:0015985	4	10.5	2.17	1.20E-03	2.20E-02	VPH1, VMA2, VMA5, ATP1, VMA6, STV1, ATP5, VMA13	18.04	8.32	
GOTERM_BP_FAT	purine ribonucleotide biosynthetic process	GO:0009152	5	13.2	1.97	1.40E-03	2.40E-02	VPH1, VMA2, VMA5, ATP1, VMA6, SPF1, STV1, PMR1, ATP5, PMC1, VMA13	9.80	4.98	
GOTERM_MF_FAT	ATPase activity, coupled vacuolar proton-transporting V-type ATPase, V1 domain	GO:0042625	7	18.4	2.11	2.60E-03	2.50E-02	VMA2, VMA5, VMA6, PMR1, VMA13	16.48	7.81	
GOTERM_CC_FAT	proton-transporting V-type ATPase, V1 domain	GO:0000221	3	7.9	3.07	1.60E-03	2.60E-02	VMA2, VMA5, VMA13	46.41	15.13	
GOTERM_BP_FAT	purine ribonucleotide metabolic process	GO:0009150	5	13.2	1.97	1.50E-03	2.60E-02	VMA2, VMA5, VMA6, PMR1, VMA13	9.53	4.84	
GOTERM_BP_FAT	ATP biosynthetic process	GO:0006754	5	13.2	1.97	2.90E-04	2.70E-02	VMA2, VMA5, VMA6, PMR1, VMA13	14.70	7.47	
GOTERM_BP_FAT	cellular ion homeostasis	GO:0006873	6	15.8	1.63	1.70E-03	2.70E-02	VCX1, VMA2, VMA5, VMA6, SOD1, VMA13	6.60	4.06	
GOTERM_BP_FAT	cellular chemical homeostasis	GO:0055082	6	15.8	1.63	1.70E-03	2.70E-02	VCX1, VMA2, VMA5, VMA6, SOD1, VMA13	6.60	4.06	
GOTERM_BP_FAT	cellular monovalent inorganic cation homeostasis	GO:0030004	4	10.5	1.93	1.90E-03	2.90E-02	VMA2, VMA5, VMA6, VMA13	15.46	8.03	
GOTERM_BP_FAT	purine nucleotide biosynthetic process	GO:0006164	5	13.2	1.97	1.90E-03	3.00E-02	VMA2, VMA5, VMA6, PMR1, VMA13	9.02	4.58	
GOTERM_BP_FAT	generation of precursor metabolites and energy	GO:0006091	8	21.1	1.73	2.30E-03	3.20E-02	VMA2, VMA5, NDI1, NDE1, YBR238C, VMA6, HXK2, VMA13	4.10	2.36	
GOTERM_BP_FAT	purine nucleotide metabolic process	GO:0006163	5	13.2	1.97	2.20E-03	3.20E-02	VMA2, VMA5, VMA6, PMR1, VMA13	8.67	4.40	
GOTERM_BP_FAT	proton transport	GO:0015992	4	10.5	2.17	2.40E-03	3.20E-02	VMA2, VMA5, VMA6, VMA13	14.24	6.57	
GOTERM_BP_FAT	hydrogen transport	GO:0006818	4	10.5	2.17	2.40E-03	3.20E-02	VMA2, VMA5, VMA6, VMA13	14.24	6.57	
GOTERM_BP_FAT	response to oxidative stress	GO:0006979	5	13.2	1.14	2.60E-03	3.20E-02	SCH9, SOD1, GAD1, SOD2, HSP104	8.25	7.23	
GOTERM_BP_FAT	ribonucleotide biosynthetic process	GO:0009152	5	13.2	1.97	2.30E-03	3.30E-02	VMA2, VMA5, VMA6, PMR1, VMA13	9.80	4.98	
GOTERM_BP_FAT	ribonucleotide metabolic process	GO:0009150	5	13.2	1.97	2.50E-03	3.30E-02	VMA2, VMA5, VMA6, PMR1, VMA13	9.53	4.84	
GOTERM_BP_FAT	monovalent inorganic cation homeostasis	GO:0030004	4	10.5	1.93	2.60E-03	3.30E-02	VMA2, VMA5, VMA6, VMA13	15.46	8.03	
GOTERM_BP_FAT	cation transport	GO:0006812	6	15.8	1.86	2.80E-03	3.30E-02	VCX1, VMA2, VMA5, VMA6, PMR1, VMA13	5.88	3.17	
GOTERM_CC_FAT	extrinsic to membrane	GO:0019898	7	18.4	2.39	2.40E-03	3.30E-02	ATG8, VMA5, TOR1, VMA6, VPS4, ATG1, VMA13	4.78	2.00	
GOTERM_BP_FAT	cellular homeostasis	GO:0019725	6	15.8	1.24	4.00E-03	4.40E-02	VPH1, NHA1, HMX1, NHX1, SPF1, TRX1, STV1, TSA1, VPS3, SOD1, PMC1, VCX1, DOT5, VMA2, AHP1, VMA5, VMA6, TSA2, TIS11, GEF1, VMA13	5.41	4.37	
GOTERM_BP_FAT	ion transmembrane transport	GO:0034220	4	10.5	2.17	3.90E-03	4.50E-02	VMA2, VMA5, VMA6, VMA13	12.02	5.55	
GOTERM_BP_FAT	replicative cell aging	GO:0001302	4	10.5	1.58	4.40E-03	4.80E-02	SCH9, HXK2, SOD2, HSP104	11.51	7.31	

Supplemental Table 5 – GO Terms significantly enriched in single gene mutant set for decreased lifespan on DR (3 of 3)

Category	Gene Ontology (GO) Term	GO Term ID	Count	Percent of Response to DR vs Mutant Set	Fold Enrichment: Positive Genes			Genes	Fold Enrichment in Positive Response to DR	Fold Enrichment in Response to DR in Total Gene Set	
					p-Value	Benjamani-test Value					
GOTERM_CC_FAT	Mitochondrial Part	GO:0044429	19	45.24	1.565934066	2.59E-08	2.95E-06	FZO1, POR1, MRPL4, TOM71, TOM70, PDA1, ALO1, PDB1, COQ4, COQ3, POSS, COO2, ATP1, PHB2, ADH3, PHB1, CYT2, MGM1, RIP1	4.313275036	2.754442304	
GOTERM_CC_FAT	Mitochondrial membrane	GO:0031966	14	33.33	1.730769231	6.31E-07	3.60E-05	FZO1, POR1, TOM71, TOM70, ALO1, COQ4, COQ3, ATP1, COQ2, PHB2, PHB1, CYT2, MGM1, RIP1	5.253143884	3.035149799	
GOTERM_CC_FAT	Mitochondrial Envelope	GO:0005740	14	33.33	1.514423077	1.80E-06	6.83E-05	FZO1, POR1, TOM71, TOM70, ALO1, COQ4, COQ3, ATP1, COQ2, PHB2, PHB1, CYT2, MGM1, RIP1	4.795020871	3.166236003	
GOTERM_CC_FAT	Mitochondrial Inner Membrane	GO:0005743	11	26.19	1.903846154	6.62E-06	1.89E-04	CQO4, COO3, FZO1, COO2, ATP1, TOM70, PHB2, PHB1, CYT2, MGM1, RIP1	5.972468392	3.137054105	
GOTERM_CC_FAT	Organelle Envelope	GO:0031967	15	35.71	1.483516484	1.11E-05	2.11E-04	FZO1, NUP170, POR1, TOM71, TOM70, ALO1, COO4, COQ3, ATP1, COQ2, PHB2, PHB1, CYT2, MGM1, RIP1	3.752245631	2.5292915	
GOTERM_CC_FAT	Envelope	GO:0031975	15	35.71	1.483516484	1.11E-05	2.11E-04	FZO1, NUP170, POR1, TOM71, TOM70, ALO1, COO4, COQ3, ATP1, COQ2, PHB2, PHB1, CYT2, MGM1, RIP1	3.752245631	2.5292915	
GOTERM_CC_FAT	Organelle Inner Membrane	GO:0019866	11	26.19	1.903846154	9.90E-06	2.26E-04	CQO4, COO3, FZO1, COO2, ATP1, TOM70, PHB2, PHB1, CYT2, MGM1, RIP1	5.709364057	2.998857889	
GOTERM_CC_FAT	Mitochondrion	GO:0005739	22	52.38	1.41025641	2.77E-05	4.51E-04	POR1, FZO1, MRPL4, TOM71, TOM70, PDA1, ALO1, PDB1, MRE11, UNG1, COQ4, COQ3, POSS, COQ2, ATP1, PHB2, ADH3, PHB1, CYT2, MGM1, MEF1, RIP1	2.369333896	1.680073126	
GOTERM_CC_FAT	Integral to Mitochondrial Membrane	GO:0032592	5	11.9	2.472527473	9.34E-05	0.001330818	POR1, COQ2, TOM71, TOM70, ALO1	19.63675214	7.941975309	
GOTERM_CC_FAT	Intrinsic to Mitochondrial Outer Membrane	GO:0031306	4	9.524	2.769230769	3.91E-04	0.004447712	POR1, TOM71, TOM70, ALO1	26.18233618	9.45473251	
GOTERM_CC_FAT	Integral to Mitochondrial Outer Membrane	GO:0031307	4	9.524	2.769230769	3.91E-04	0.004447712	POR1, TOM71, TOM70, ALO1	26.18233618	9.45473251	
GOTERM_CC_FAT	Mitochondrial Membrane Part	GO:0044455	7	16.67	1.514423077	5.52E-04	0.005701644	POR1, COQ2, ATP1, TOM71, ALO1, RIP1	6.443309295	4.25462963	
GOTERM_BP_FAT	Oxidation Reduction	GO:0055114	13	30.95	1.545731707	1.52E-05	0.006354559	POR1, TSA1, PDA1, PDB1, ALO1, COQ4, GPX1, ATP1, ADH1, PHB2, ADH3, PHB1, RIP1	4.374352242	2.829955691	
GOTERM_BP_FAT	Oxidoreduction Coenzyme Metabolic Process	GO:0006733	6	14.29	2.536585366	1.43E-04	0.029566459	CQO4, COQ3, POSS, COQ2, ADH1, ADH3	11.31242741	4.45970696	
SP_PIR_KEY_WORDS	mitochondrion	na	21	50	1.848837209	1.44E-09	1.76E-07	FZO1, POR1, MRPL4, TOM71, TOM70, PDA1, ALO1, PDB1, UNG1, COQ4, COQ3, POSS, COQ2, ATP1, PHB2, ADH3, PHB1, CYT2, MGM1, MEF1, RIP1	4.553672316	2.462992574	
SP_PIR_KEY_WORDS	transit peptide	na	13	30.95	1.822751323	5.11E-07	3.11E-05	MRPL4, PDA1, PDB1, UNG1, COQ4, COQ3, ATP1, COQ2, POSS, ADH3, MEF1, MGM1, RIP1	6.084785134	3.338242062	
SP_PIR_KEY_WORDS	Mitochondrion Inner Membrane	na	8	19.05	2.523809524	1.14E-04	0.00463801	COQ4, COQ3, COQ2, ATP1, PHB2, PHB1, CYT2, MGM1	6.861399308	2.71866765	
SP_PIR_KEY_WORDS	Ubiquinone Biosynthesis	na	3	7.143	3.785714286	0.00107	82	0.025978775	GPX1, ADH1, ADH3, TSA1, PDA1, PDB1, ALO1, RIP1	57.57142857	15.20754717
SP_PIR_KEY_WORDS	Oxidoreductase	na	8	19.05	1.442176871	9.88E-04	0.029703169	MRPL4, PDA1, PDB1, UNG1, COQ4, COQ3, ATP1, COQ2, POSS, ADH3, MEF1, MGM1, RIP1	4.81643324	3.339696633	
UP_SEQ_FEATURE	transit peptide:Mitochondrion	na	13	30.95	1.822751323	4.62E-07	5.13E-05	SGS1, RAD55, RAD51, MRE11	6.140952381	3.369056604	
KEGG_PATHWAY	Homologous Recombination	sce03440	4	9.524	1.742857143	0.00165	66	0.029402617	15.14736842	8.691113028	

Supplemental Table 6 – GO terms significantly enriched in single gene mutant set for positive response to DR

Short Genotype	2% Glucose		0.5% Glucose		0.1% Glucose		0.05% Glucose		3% Glycerol		3% Ethanol	
	N	Mean RLS	N	Mean RLS	N	Mean RLS	N	Mean RLS	N	Mean RLS	N	Mean RLS
BY4742	4317	25.5	579	26.2	378	28.1	3727	27.3	719	25.6	100	31.7
<i>phb1Δ</i>	573	13.8	138	15.0	20	24.1	389	24.8	114	27.8	60	32.3
<i>phb2Δ</i>	577	14.0	100	15.7	99	23.5	388	25.5	137	30.6	39	32.4
<i>sod2Δ</i>	443	27.6	192	15.8	39	13.5	290	5.9	179	7.1	74	4.4

Supplemental Table 7 – Mean Replicative Lifespans of BY4742, *sod2Δ*, *phb1Δ*, and *phb2Δ* on fermentable and non-fermentable carbon sources

Strain	Short Genotype	Long Genotype	2% Glucose		0.05% Glucose		Source
			N	Mean RLS	N	Mean RLS	
JS1003	<i>sod2Δ hap4Δ</i>	MATalpha sod2::KANMX hap4::KANMX LYS2 MET15 leu2D0 his3D0 ura3D0 lys2D0 met15D0	60	23.6	80	26.3	This study
JS1004	<i>sod2Δ rip1Δ</i>	MATalpha sod2::KANMX rip1::KANMX leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	26.2	80	17.0	This study
JS590	<i>phb1Δ hap4Δ</i>	MATalpha hap4::KANMX phb1::KANMX LYS2 leu2D0 his3D0 ura3D0 lys2D0 met15D0	60	14.3	60	18.8	This study
JS592	<i>phb2Δ hap4Δ</i>	MATalpha hap4::KANMX phb2::KANMX leu2D0 his3D0 ura3D0 lys2D0 met15D0	39	10.9	60	23.4	This study
JS861	<i>phb1Δ rip1Δ</i>	MATalpha rip1::KANMX phb1::KANMX MET15 leu2D0 his3D0 ura3D0 lys2D0 met15D0	40	14.0	40	23.9	This study
JS862	<i>phb1Δ rip1Δ</i>	MATalpha rip1::KANMX phb1::KANMX LYS2 leu2D0 his3D0 ura3D0 lys2D0 met15D0	40	11.0	40	24.6	This study
JS866	<i>phb2Δ rip1Δ</i>	MATalpha rip1::KANMX phb2::KANMX MET15 leu2D0 his3D0 ura3D0 lys2D0 met15D0	40	10.7	40	22.1	This study
JS118	<i>phb1Δ atg13Δ</i>	MATalpha atg13::KANMX phb1::KANMX MET15 leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	12.9	20	19.3	This study
JS134	<i>phb1Δ atg13Δ</i>	MATalpha atg13::KANMX phb1::KANMX leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	13.0	20	18.8	This study
JS283	<i>phb2Δ atg13Δ</i>	MATalpha atg13::KANMX phb2::KANMX MET15 leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	16.5	20	27.3	This study
JS114	<i>phb2Δ atg13Δ</i>	MATalpha atg13::KANMX phb2::KANMX MET15 leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	17.1	20	28.3	This study
JS115	<i>phb2Δ atg13Δ</i>	MATalpha atg13::KANMX phb2::KANMX leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	14.6	20	24.2	This study
JS956	<i>phb1Δ atg32Δ</i>	MATalpha atg32::KANMX phb1::KANMX leu2D0 his3D0 ura3D0 lys2D0 met15D0	40	14.0	40	27.6	This study
JS961	<i>phb1Δ atg32Δ</i>	MATalpha atg32::KANMX phb1::KANMX LYS2 leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	9.8	20	23.3	This study
JS958	<i>phb2Δ atg32Δ</i>	MATalpha atg32::KANMX phb2::KANMX MET15 leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	12.8	20	27.3	This study
JS959	<i>phb2Δ atg32Δ</i>	MATalpha atg32::KANMX phb2::KANMX LYS2 leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	13.3	20	28.5	This study
JS962	<i>phb2Δ atg32Δ</i>	MATalpha atg32::KANMX phb2::KANMX leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	10.7	20	25.6	This study
JS766	<i>phb1Δ sch9Δ</i>	MATalpha sch9::HIS3 phb2::KANMX LYS2 leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	25.5			This study
JS767	<i>phb1Δ sch9Δ</i>	MATalpha sch9::HIS3 phb2::KANMX LYS2 MET15 leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	26.8			This study
JS542	<i>phb2Δ sch9Δ</i>	MATalpha sch9::HIS3 phb2::KANMX LYS2 MET15 leu2D0 his3D0 ura3D0 lys2D0 met15D0 his3D0	20	24.8			This study
JS543	<i>phb2Δ sch9Δ</i>	MATalpha sch9::HIS3 phb2::KANMX leu2D0 ura3D0 met15D0 Lys2D0 his3D0	20	26.2			This study
JS305	<i>phb1Δ rpl20bΔ</i>	MATalpha rpl20b::HIS3 phb1::KANMX LYS2 leu2D0 his3D0 ura3D0 met15D0 lys2D0	40	30.8			This study
JS309	<i>phb1Δ rpl20bΔ</i>	MATalpha rpl20b::HIS3 phb1::KANMX leu2D0 his3D0 ura3D0 met15D0 lys2D0	20	26.3			This study
JS312	<i>phb1Δ rpl20bΔ</i>	MATalpha rpl20b::HIS3 phb1::KANMX LYS2 leu2D0 his3D0 ura3D0 met15D0 lys2D0	20	24.3			This study
JS1240	<i>phb1Δ rpl20bΔ gcn4Δ</i>	MATalpha rpl20b::HIS3 gcn4::KANMX phb2::KANMX MET15 leu2D0 his3D0 ura3D0 lys2D0 met15D0	40	28.3			This study
JS1241	<i>phb1Δ rpl20bΔ gcn4Δ</i>	MATalpha rpl20b::HIS3 gcn4::KANMX phb2::KANMX leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	22.0			This study
JS836	<i>rps7aΔ</i>	MATalpha rps7a::KANMX LYS2 leu2D0 his3D0 ura3D0 met15D0 lys2D0	40	21.0			Deletion Collection
JS885	<i>phb1Δ rps7aΔ</i>	MATalpha rps7a::KANMX phb2::KANMX leu2D0 ura3D0 met15D0 Lys2D0 his3D0	20	19.0			This study
JS306	<i>phb2Δ rpl20bΔ</i>	MATalpha rpl20b::HIS3 phb2::KANMX MET15 leu2D0 his3D0 ura3D0 met15D0 lys2D0	20	22.8			This study
JS308	<i>phb2Δ rpl20bΔ</i>	MATalpha rpl20b::HIS3 phb2::KANMX MET15 leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	24.1			This study
JS1151	<i>phb2Δ rpl20bΔ</i>	MATalpha rpl20b::HIS3 phb2::KANMX leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	23.9			This study
JS1152	<i>phb2Δ rpl20bΔ</i>	MATalpha rpl20b::HIS3 phb2::KANMX leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	25.0			This study
JS1162	<i>phb2Δ rpl20bΔ</i>	MATalpha rpl20b::HIS3 phb2::KANMX MET15 leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	28.0			This study
JS1143	<i>phb2Δ rpl20bΔ gcn4Δ</i>	MATalpha rpl20b::HIS3 gcn4::KANMX phb2::KANMX leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	17.1			This study
JS1144	<i>phb2Δ rpl20bΔ gcn4Δ</i>	MATalpha rpl20b::HIS3 gcn4::KANMX phb2::KANMX LYS2 leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	17.6			This study
JS1145	<i>phb2Δ rpl20bΔ gcn4Δ</i>	MATalpha rpl20b::HIS3 gcn4::KANMX phb2::KANMX LYS2 leu2D0 his3D0 ura3D0 lys2D0 met15D0	80	19.9			This study
JS1147	<i>rpl20bΔ gcn4Δ</i>	MATalpha rpl20b::HIS3 gcn4::KANMX MET15 LYS2 leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	30.9			This study
JS1148	<i>rpl20bΔ gcn4Δ</i>	MATalpha rpl20b::HIS3 gcn4::KANMX MET15 leu2D0 his3D0 ura3D0 lys2D0 met15D0	20	31.5			This study

Table S8 – Full genotype and RLS data of double mutant strains tested.

	2% Glu		0.05% Glu		2% Glu + 6mM NAC		0.05% Glu + 6mM NAC	
Strain	N	Mean RLS	N	Mean RLS	N	Mean RLS	N	Mean RLS
sod1 α	50	2.5	33	2.6	51	17.5	56	20.6
sod2 α	56	26.2	49	7.5	59	24.7	60	20.4

Supplemental Table 9 – Mean Replicative Lifespans of *sod1 Δ* and *sod2 Δ* on 2% glucose and 0.05% glucose medias with and without 6mM N-acetylcysteine (NAC)

p-value PHB q-value PHB				p-value PHBq-value PHB				p-value PHB q-value PHB			
Common Name		Fasta ID		Pooled to BY on YPD		Pooled to BY on YPD		Common Name		Fasta ID	
TIF5	YPR041W	6.23E-07	1.75E-04	KRS1	YDR037W	5.03E-03	1.94E-02	FAS2	YPL231W	2.12E-02	4.12E-02
ERG27	YLR100W	1.36E-72	1.91E-70	MAP1	YLR244C	5.38E-03	2.02E-02	BA11	YHR208W	2.15E-02	4.15E-02
MET6	YER091C	8.63E-06	8.10E-04	ERG13	YML126C	5.46E-03	2.02E-02	RPL11B	YGR085C	2.20E-02	4.21E-02
LEU4	YNL104C	3.11E-05	1.99E-03	FAS1	YKL182W	5.53E-03	2.02E-02	ZE01	YOL109W	2.22E-02	4.22E-02
RP57A	YOR096W	3.54E-05	1.99E-03	PAM18	YLR008C	5.53E-03	2.02E-02	NCP1	YHR042W	2.24E-02	4.23E-02
COX4	YGL187C	6.66E-05	2.40E-03	ILV3	YJR016C	6.03E-03	2.18E-02	TFP3	YPL234C	2.36E-02	4.44E-02
ILS1	YBL076C	6.84E-05	2.40E-03	ABP1	YCR088W	6.18E-03	2.18E-02	RPS18A	YDR450W		
HSP10	YOR020C	7.02E-05	2.40E-03	ADO1	YJR105W	6.20E-03	2.18E-02	RPS18B	YML026C	2.43E-02	4.51E-02
MMF1	YIL051C	7.66E-05	2.40E-03	ARC1	YGL105W	6.55E-03	2.27E-02	RPS19A	YOL121C	2.43E-02	4.51E-02
WBP1	YEL002C	9.58E-05	2.65E-03	ALD4	YOR374W	1.04E-04	2.65E-03	SRO9	YCL037C	2.48E-02	4.56E-02
ALD4	YOR374W	1.04E-04	2.65E-03	ALD5	YER073W	6.68E-03	2.27E-02	VTC4	YJL012C	2.52E-02	4.60E-02
QCR7	YDR529C	1.22E-04	2.65E-03	HEM15	YOR176W	6.89E-03	2.27E-02	RPL19B	YBR084C-A		
SEC21	YNL287W	1.22E-04	2.65E-03	URA1	YKL216W	6.93E-03	2.27E-02	RPL19A	YBL027W	2.58E-02	4.67E-02
TY51	YGR185C	1.57E-04	3.03E-03	HSP78	YDR258C	7.10E-03	2.27E-02	DED81	YHR019C	2.59E-02	4.67E-02
TIM9	YEL020W-A	1.82E-04	3.03E-03	RPS1A	YLR441C	7.10E-03	2.27E-02	CAR2	YLR438W	2.63E-02	4.68E-02
THR4	YCR053W	1.82E-04	3.03E-03	ERG26	YGL001C	7.25E-03	2.27E-02	ETR1	YBR026C	2.63E-02	4.68E-02
MDH1	YKL085W	1.83E-04	3.03E-03	TIF3	YPR163C	7.25E-03	2.27E-02	SCW4	YGR279C	2.65E-02	4.69E-02
RPL12A	YEL054C-Y			RPL4B	YDR012W	7.26E-03	2.27E-02	SEC13	YLR208W	2.76E-02	4.86E-02
RPL12B	DR418W	3.23E-04	4.62E-03	ACH1	YBL015W	7.50E-03	2.27E-02	FRS1	YLR060W	2.82E-02	4.92E-02
RPL13A	YDL082W	3.23E-04	4.62E-03	PDR5	YOR153W	7.50E-03	2.27E-02	FPR4	YLR449W	2.92E-02	5.02E-02
POL2	YNL262W	3.30E-04	4.62E-03	RPL4A	YBR031W	7.50E-03	2.27E-02	RIM1	YCR028C-A	2.92E-02	5.02E-02
ADH1	YOL086C	3.53E-04	4.62E-03	SGT2	YOR007C	7.51E-03	2.27E-02	RIP1	YEL024W	2.92E-02	5.02E-02
LEU9	YOR108W	3.61E-04	4.62E-03	CPR3	YML078W	7.79E-03	2.33E-02	GLN1	YPR035W	2.94E-02	5.02E-02
PRE6	YOL038W	4.86E-04	5.85E-03	SWP1	YMR149W	8.16E-03	2.42E-02	ATP5	YDR298C	2.99E-02	5.08E-02
NUG1	YER006W	4.98E-04	5.85E-03	LPD1	YFL018C	8.36E-03	2.45E-02	RPL26A	YLR344W	3.06E-02	5.13E-02
ADE17	YMR120C	6.94E-04	7.78E-03	HOM2	YDR158W	9.35E-03	2.58E-02	TSA1	YML028W	3.06E-02	5.13E-02
ATP3	YBR039W	7.69E-04	7.78E-03	URA5	YML106W	9.35E-03	2.58E-02	VTCA	YER072W	3.19E-02	5.27E-02
RPS15	YOL040C	7.71E-04	7.78E-03	GLK1	YCL040W	9.63E-03	2.61E-02	RPL25	YOL127W	3.19E-02	5.27E-02
ALD6	YPL061W	8.05E-04	7.78E-03	TPS1	YBR126C	9.63E-03	2.61E-02	ACO1	YLR304C	3.29E-02	5.27E-02
PRS5	YOL061W	8.05E-04	7.78E-03	YBR118W-Y				CIR2	YOR356W	3.31E-02	5.27E-02
GLN4	YOR168W	8.30E-04	7.78E-03	TEF1,TEF2	PR080W	9.17E-03	2.58E-02	HOM2	YDR158W	9.35E-03	2.58E-02
PTC3	YPL019C	8.99E-04	7.93E-03	CIR1	YGR207C	9.35E-03	2.58E-02	ATP2	YER121W	9.02E-03	2.58E-02
ATP2	YER121W	9.02E-04	7.93E-03	HOM2	YDR158W	9.35E-03	2.58E-02	SHM1	YBR263W	3.31E-02	5.27E-02
CDC60	YPL160W	9.60E-04	8.19E-03	GLK1	YCL040W	9.63E-03	2.61E-02	TM13	YGR181W	3.31E-02	5.27E-02
MGE1	YOR232W	1.07E-03	8.62E-03	TPS1	YBR126C	9.63E-03	2.61E-02	URA2	YJL130C	3.31E-02	5.27E-02
KGD2	YDR148C	1.08E-03	8.62E-03	RPS3	YNL178W	1.06E-02	2.74E-02	YLR256W-A		3.31E-02	5.27E-02
SPF1	YEL031W	1.13E-03	8.62E-03	GUAI1	YMR217W	1.06E-02	2.74E-02	RPS4A	YHR203C		
TIF35	YDR429C	1.13E-03	8.62E-03	RPS19B	YNL302C	1.11E-02	2.74E-02	RPS4B	YJR145C	3.40E-02	5.32E-02
IDH2	YOR136W	1.17E-03	8.62E-03	ADE1	YAR015W	1.12E-02	2.74E-02	MIS1	YBR084W	3.42E-02	5.32E-02
RPL2B,R	YFR031C-P			YPS1	YML030W	1.12E-02	2.74E-02	RPA190	YOR341W	3.42E-02	5.32E-02
PL2A	A,YL018W	1.22E-03	8.62E-03	FPR2	YDR519W	1.12E-02	2.74E-02	TMA19	YKL056C	3.42E-02	5.32E-02
PET9	YBL030C	1.23E-03	8.62E-03	HAS1	YMR290C	1.12E-02	2.74E-02	RPL16B	YNL069C	3.63E-02	5.61E-02
TKL1	YPR074C	1.36E-03	9.32E-03	HCH1	YNL281W	1.12E-02	2.74E-02	LYS12	YIL094C	3.74E-02	5.68E-02
ILV2	YMR108W	1.42E-03	9.49E-03	HIS4	YCL030C	1.12E-02	2.74E-02	BMH2	YDR099W	3.79E-02	5.68E-02
CHC1	YGL206C	1.57E-03	1.03E-02	MDJ1		1.12E-02	2.74E-02	PDB1	YBR221C	3.82E-02	5.68E-02
KAP123	YER110C	1.72E-03	1.10E-02	YOL103W-B				RPL21B	YPL079W	3.82E-02	5.68E-02
IDH1	YNL037C	1.75E-03	1.10E-02	ALA1	YOR35C	1.21E-02	2.93E-02	CBF5	YLR175W	3.83E-02	5.68E-02
MET17	YLR303W	1.90E-03	1.14E-02	RPS7B	YNL096C	1.22E-02	2.93E-02	GRX5	YPL059W	3.83E-02	5.68E-02
RPL17A	YKL180W	1.90E-03	1.14E-02	ADE3	YGR204W	1.23E-02	2.93E-02	PMT1	YDL095W	3.83E-02	5.68E-02
LSC1	YOR142W	1.98E-03	1.15E-02	VMA8	YEL051W	1.25E-02	2.93E-02	TSR2		3.83E-02	5.68E-02
YSA1	YBR111C	2.01E-03	1.15E-02	IMD5	YLR432W	1.25E-02	2.93E-02	STE24	YJR117W	3.89E-02	5.73E-02
PDA1	YER178W	2.15E-03	1.21E-02	SBA1	YKL117W	1.26E-02	2.93E-02	SAG1	YJR004C	3.92E-02	5.75E-02
ILV5	YLR355C	2.34E-03	1.25E-02	PYC2	YBR218C	1.30E-02	3.00E-02	NEW1	YPL226W	3.97E-02	5.79E-02
KGD1	YIL125W	2.39E-03	1.25E-02	CLU1	YMR012W	1.38E-02	3.15E-02	SMT3	YDR510W	4.07E-02	5.82E-02
ACC1	YNR016C	2.50E-03	1.25E-02	RPS1B	YML063W	1.48E-02	3.35E-02	ERG6	YML008C	4.11E-02	5.82E-02
SER33	YIL074C	2.50E-03	1.25E-02	TOM22	YNL131W	1.49E-02	3.35E-02	PCY1	YGL062W	4.12E-02	5.82E-02
CAR1	YPL111W	2.54E-03	1.25E-02	RPL14B	YHL001W	1.50E-02	3.35E-02	ZPR1	YGR211W	4.12E-02	5.82E-02
FUN12	YAL035W	2.54E-03	1.25E-02	SSC1	YJR045C	1.52E-02	3.38E-02	EGD1	YPL037C	4.13E-02	5.82E-02
GCV3	YAL044C	2.54E-03	1.25E-02	RPS31	YLR167W	1.60E-02	3.52E-02	RTN2	YDL204W	4.13E-02	5.82E-02
ILV1	YER086W	2.79E-03	1.33E-02	COR1	YBL045C	1.62E-02	3.53E-02	TIM50	YPL063W	4.13E-02	5.82E-02
GCV1	YDR019C	2.80E-03	1.33E-02	HOR2	YER062C	1.68E-02	3.59E-02	GSF2	YML048W	4.18E-02	5.85E-02
YHM2	YMR241W	2.83E-03	1.33E-02	RN41	YGR180C	1.68E-02	3.59E-02	YBR012W-B		4.22E-02	5.88E-02
HSP60	YLR259C	3.10E-03	1.43E-02	PRL28	YGL103W	1.68E-02	3.59E-02	LAT1	YNL071W	4.24E-02	5.88E-02
ATP1	YBL099W	3.24E-03	1.47E-02	RPL43A	YPR043W	1.69E-02	3.59E-02	MIR1	YJR077C	4.41E-02	6.09E-02
PFK1	YGR240C	3.62E-03	1.60E-02	YJR094W-A		1.73E-02	3.67E-02	OST3		4.44E-02	6.09E-02
SEC4	YFL005W	3.67E-03	1.60E-02	ACS2	YLR153C	1.76E-02	3.71E-02	GCV2	YMR189W	4.52E-02	6.17E-02
TUF1	YOR187W	3.70E-03	1.60E-02	ARO8	YGL202W	1.90E-02	3.93E-02	RPL14A	YKL006W	4.56E-02	6.20E-02
GDH1	YOR375C	3.82E-03	1.63E-02	SOD1	YJR104C	1.90E-02	3.93E-02	OLA1	YBR025C	4.64E-02	6.24E-02
SSB2	YNL209W	3.95E-03	1.66E-02	MAE1	YKL029C	1.99E-02	3.95E-02	PNC1	YGL037C	4.64E-02	6.24E-02
CCT8	YJL008C	4.68E-03	1.87E-02	CIT1	YNR001C	1.99E-02	3.95E-02	ADE6	YGR061C	4.68E-02	6.24E-02
CWP1	YKL096W	4.72E-03	1.87E-02	DYS1	YHR068W	1.99E-02	3.95E-02	CPR1	YDR155C	4.68E-02	6.24E-02
GLY1	YEL046C	4.72E-03	1.87E-02	FMP41	YNL168C	1.99E-02	3.95E-02	ILV6	YCL009C	4.73E-02	6.24E-02
TIM8	YJR135W-A	4.72E-03	1.87E-02	GCN20	YFR009W	1.99E-02	3.95E-02	SEC28	YIL076W	4.74E-02	6.24E-02
GCD11	YER025W	4.92E-03	1.93E-02	PDC6	YGR087C	1.99E-02	3.95E-02	ERP1	YAR002C-A	4.79E-02	6.24E-02
			RPL43B	YKR094C	2.09E-02	4.12E-02	YKL033W-A		4.79E-02	6.24E-02	
			RPL40B	YKR094C	2.11E-02	4.12E-02	NOP58	YOR310C	4.81E-02	6.24E-02	
			RPL40A	YIL148W	2.11E-02	4.12E-02	YPT53	YNL093W	4.81E-02	6.24E-02	
							IMD4	YML056C	4.92E-02	6.35E-02	

Supplemental Table 10 - Pooled Spectral Count Data from *phb1Δ* and *phb2Δ* cells compared to WT - Targets differing from WT in on 2% glucose and rescued on 3% glycerol.

Swiss Protein Keyword - Molecular Function

Category: SP_PIR_KEYWORDS

Term	Count	% of Targets	P-Value	Benjamini
Transit peptide	41	22.8	4.90E-16	3.50E-14
Oxidoreductase	35	19.4	7.10E-15	4.20E-13
Mitochondrion	56	31.1	2.70E-13	1.30E-11
Acetylation	23	12.8	5.70E-10	1.90E-08
NAD	16	8.9	1.30E-08	3.20E-07
Amino-acid biosynthesis	15	8.3	3.60E-07	7.20E-06
Branched-chain amino acid biosynthesis	7	3.9	6.10E-07	1.10E-05
Chaperone	14	7.8	9.60E-07	1.50E-05
Nucleotide-binding	43	23.9	2.50E-06	3.60E-05
Tricarboxylic acid cycle	8	4.4	8.20E-06	1.00E-04
NADP	12	6.7	1.60E-05	1.90E-04
ATPbinding	36	20	4.80E-05	5.20E-04
Multifunctional enzyme	11	6.1	7.20E-05	7.40E-04
Ubl conjugation	15	8.3	8.00E-05	7.90E-04
Purine biosynthesis	6	3.3	1.30E-04	1.30E-03
Membrane-associated complex	7	3.9	2.10E-04	1.90E-03
Thiamine pyrophosphate	5	2.8	2.40E-04	2.10E-03
Mitochondrion inner membrane	15	8.3	4.20E-04	3.40E-03
Metal-binding	34	18.9	4.40E-04	3.50E-03
ATP	17	9.4	1.10E-03	7.60E-03
Flavoprotein	8	4.4	2.20E-03	1.40E-02
Hydrogen ion transport	6	3.3	2.60E-03	1.60E-02
Carbon-oxygen lyase	5	2.8	2.80E-03	1.70E-02
Purine nucleotide biosynthesis	4	2.2	2.90E-03	1.70E-02
Molecular chaperone	5	2.8	3.40E-03	1.90E-02
Thiamin pyrophosphate	3	1.7	4.40E-03	2.30E-02
ATP biosynthesis	4	2.2	4.90E-03	2.50E-02
Oxo-acid-lyase	4	2.2	4.90E-03	2.50E-02
Nucleotide binding	11	6.1	5.40E-03	2.70E-02
Methionine biosynthesis	5	2.8	6.10E-03	3.00E-02
Oxidative phosphorylation	5	2.8	7.00E-03	3.30E-02
Peripheral membrane protein	3	1.7	7.30E-03	3.40E-02
ATP synthesis	4	2.2	7.50E-03	3.40E-02

Supplemental Table 11 – Gene ontology (GO) analysis of statistically significant targets.

Strain	RNAi treatment	Median Lifespan	Mean Lifespan	N	SEM	p-value (vs. N2 EV RNAi)	p-value (vs. EV RNAi)
N2	<i>EV</i>	23	23.3	83	0.3	NA	NA
	<i>phb-2</i>	20	20.1	98	0.5	1.1E-06	1.1E-06
N2	<i>EV</i>	20	21.1	112	0.4	NA	NA
	<i>phb-2</i>	17	18.7	96	0.7	7.2E-03	7.2E-03
<i>rsks-1 (ok1255)</i>	<i>EV</i>	26	25.7	105	0.7	NA	NA
	<i>phb-2</i>	26	26.7	107	0.8	NA	7.9E-01
<i>rsks-1 (ok1255)</i>	<i>EV</i>	25	24.4	150	0.5	NA	NA
	<i>phb-2</i>	29	28.2	152	0.7	NA	1.7E-05
<i>rsks-1 (ok1255)</i>	<i>EV</i>	27	25.4	171	0.4	NA	NA
	<i>phb-2</i>	25	25.2	140	0.6	NA	6.3E-01
Total							
N2	<i>EV</i>	23	22.9	309	0.2	NA	NA
	<i>phb-2</i>	21	20.5	310	0.3	2.1E-07	2.1E-07
<i>rsks-1 (ok1255)</i>	<i>EV</i>	26	24.7	522	0.3	2.8E-06	NA
	<i>phb-2</i>	27	26.6	543	0.3	2.5E-07	3.6E-03

Supplemental Table 12 – *C. elegans* life span data. Animals lost to foraging were not included.